UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | MAY 2004

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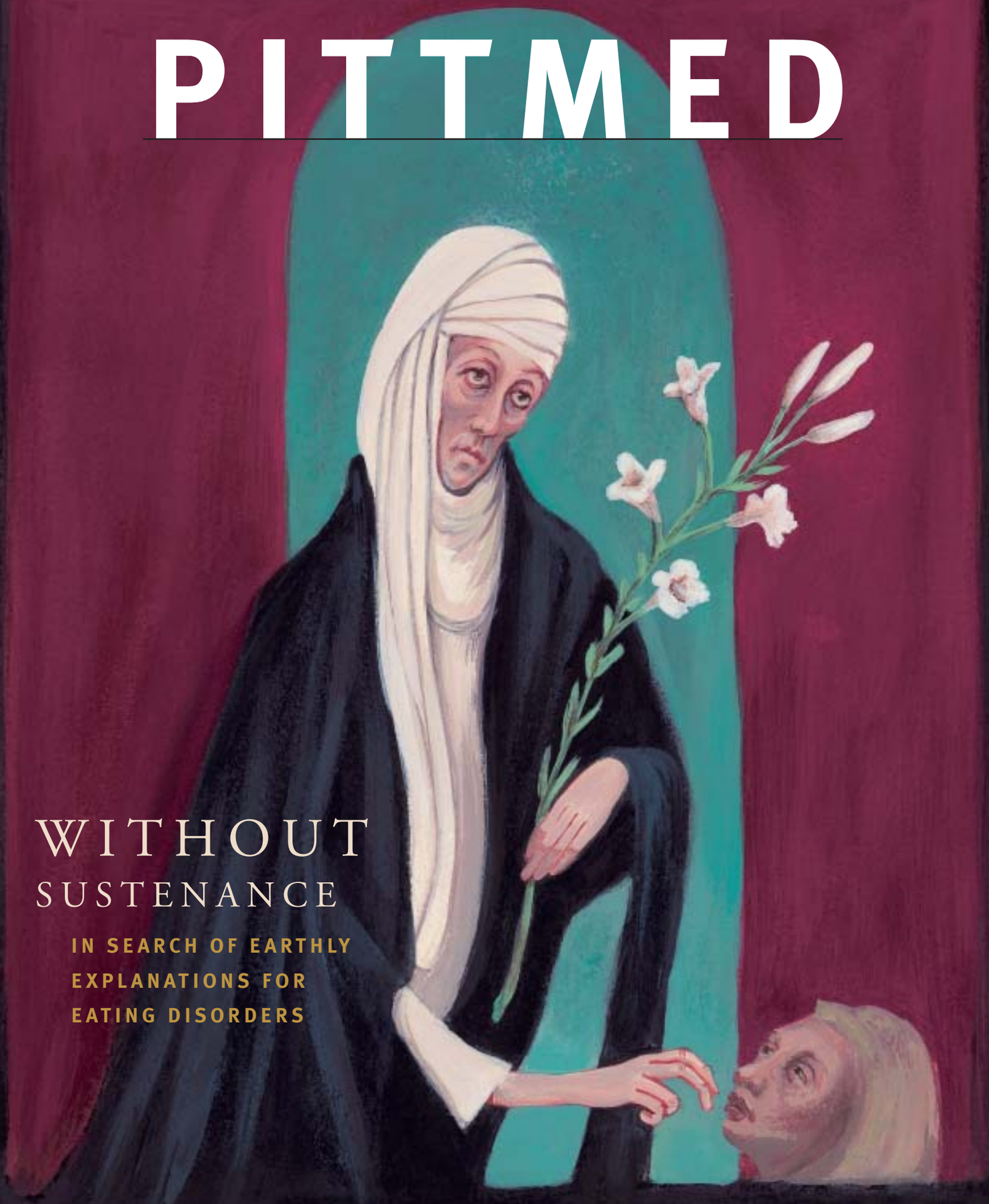

WITHOUT SUSTENANCE

IN SEARCH OF EARTHLY EXPLANATIONS FOR EATING DISORDERS

PITTMED PM MAY 2004

WHODUNNIT

We had many responses from the February Last Call (shown right). Trying to identify those pictured was a trip down memory lane for some and pure speculation for others.

Joe Hakas (MD '57) identified the suspects as follows: Clockwise from left—Mickey Zernich (sitting); Doug Hardy (using stethoscope); Phil Levine; Herb Cronin; Al Winters.

Edward Jew (MD '53) also called. Referring us to the 1953-54 Hippocratean, *he noted the caption said "PMB"–i.e., "poor miserable bastard." He says it was a posed picture with (clockwise from left) Marshall Levy (MD '53), now deceased (sitting); Dr. Jew himself (bending with stethoscope); Leo King (MD '53); Jake Fong (MD '53) (holding tongue blade); Pat Hughes (MD '53) (patient/PMB); and the late Charles Johns (MD '53) (wrapping ankle). Dr. Jew notes that Marshall Levy was the editor of* The Hippocratean *and Mervin Stewart (MD '53) probably took the photo.*

James Bates (MD '53) phoned and concurred with Dr. Jew's description, though he didn't recognize Hughes/PMB. And we got mail:

I believe that the physician in the foreground taping the patient's ankle looks similar to Dr. Withers, who is on staff at Mercy Hospital.

Marc Reichel, MD
Beaufort, S.C.

I am certain that by now many of the Class of '53 have responded to your request for the names of the people on page 40 of your excellent journal. The original picture appears on page 119 of the 1953–54 *Hippocratean.* I would bet that Mervin Stewart took the original photograph!

Those pictured are, clockwise from the top, Leo King, Jake Fong, Charles Johns, Marshall Levy, and Edward Jew. I am not sure who the victim (excuse me, patient) was—but it was not me!

Henry J. Mankin (MD '53)
Harvard Medical School

The photograph was taken by me for *The Hippocratean* yearbook (1953). It was probably taken in the orthopaedic clinic at Falk with my classmates horsing around for the photo. Leo King is at the top of the photo steadying patient Arthur Larson's head. Marshall Levy is seated to the left, pointing his finger as he directs his classmate's care. Charles Johns is bandaging the foot. Edward Jew may be the person with the stethoscope, and Robert Lewine could be the classmate with the tongue blade.

Mervin S. Stewart (MD '53)
University of Pittsburgh

Dr. Stewart, who still has an irresistible touch with a shutter, also sent this photo from his reunion last year, suggesting the title, "We Had So Much to Talk About."

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

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

Women in Communications
- Matrix Award, Feature Writing (Ed Kiester's "Drowning in Their Own Blood")
- Honorable Mention, Feature Writing (Chuck Staresinic's "Pirated Genes")

HOW DO YOU LIKE YOUR EGGS?

Try them in good company and with a side of scintillating speakers at this year's Dean's Breakfast.

In addition to our headliner, Dean Arthur S. Levine, you'll meet three stellar Pitt medical students, including an MD/PhD student and the president of the Student National Medical Association. And you'll get to know SimMan, a humanoid who's part of the reason Pitt is among the very best places to get a medical education today.

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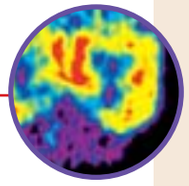

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Giving birth to a 50-year-old—these are golden times for Scope and Scalpel.
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CONTRIBUTORS

There aren't too many things that could bring DAVID R. ELTZ ["Rack 'Em Up"] to Pittsburgh from Florida's Gulf Coast in the middle of winter. Lucky for us, the chance to stretch his literary legs for a *Pitt Med* feature was one of them. Our former senior editor now oversees a bevy of health-related publications in Venice, a stone's throw from where his beloved Yankees came this March to soak up 80-degree sunshine during spring training.

LINDA WALLEN [Cover] never knows what offerings from strangers might show up in her mail. She has gotten cobalt blue glass chunks from West Virginia, a ceramic angel from New Mexico, and broken Quimper vials from France. So far, she's always been able to incorporate what she receives into the ceramic mosaics she's creating on the outside and inside of her home in Pittsburgh's Spring Hill neighborhood. Wallen holds degrees in art from Indiana University Bloomington and the University of Iowa. Regarding the mosaic that now covers a third of the front of her house, she says, "It's an effort to make Pittsburgh a little prettier around the edges, or at least more interesting."

COVER

Catherine of Siena (1347–1380) showed her devotion to God by denying herself food. Today, she's thought to have had anorexia nervosa, as are other saints. What's the biological link among young adults who've starved themselves through the centuries? (The cover painting by Linda Wallen is a modern interpretation of a late 14th-century fresco of St. Catherine by Vanni in the Church of San Domenico in Siena, Italy. © Linda Wallen.)

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JULIA MAROUS STRAUT

No social advance rolls in on the wheels of inevitability. This is no time for apathy or complacency; this is a time for vigorous and positive social action.
—Martin Luther King Jr.

Few would have questioned Matthew Neal and James Starman if they had focused exclusively on their studies and the torrent of exams facing them in their second year here at the School of Medicine. Instead, Matthew and James, while sustaining their notable academic progress, mobilized medical students across the commonwealth to take action on an issue that threatens to greatly compromise health care for many Pennsylvanians. In February, they sent a petition with 1,251 medical student signatures to Governor Edward Rendell. At issue: Medical malpractice insurance premiums in Pennsylvania soared 40 percent in 2002 alone (while rising 15 percent nationally), and they continue to rise. An obstetrician, for example, is likely to be faced with $135,000 or more in premium payments each year. This has had dire consequences. More than 1,400 physicians have closed their offices, left the state, or limited their services because of malpractice insurance costs. Those who stayed were more likely to be lured into the practice of defensive medicine (i.e., hoping to avoid liability by ordering expensive and sometimes unnecessary tests or dropping out of "high risk" areas, such as delivering babies). Students couldn't imagine how they could establish a practice in Pennsylvania; and many were heartbroken at the thought that they wouldn't be able to make a go of it in communities they loved, particularly when those graduating in 2004 expected to assume medical school debts of almost $140,000 (the average at Pitt). Matthew and James requested a meeting with the governor to discuss these issues as well as how to address physician errors that are likely to emerge when economically driven time constraints have become so severe.

Health care is broken in so many ways in this country: 44 million uninsured, skyrocketing costs, declining financial support for academic medical centers that care for the indigent and uninsured, lack of physicians in rural areas, politicized research agendas … It is my view that physicians themselves contributed to this mess: Doctors as a group for so long were resistant to embrace Medicare or any changes to the system that might involve the fair and rational control of, and compensation for, healthcare expenses. We removed ourselves from the discussion and let others assume the responsibility and authority to take on issues that needed our unique expertise and insight. Yet it's our responsibility as physicians to be stewards of the health of this country, and it's time that we reclaimed leadership and authority. (In these troubling times, it's helpful to remember that a kick in the behind eventuates in a step forward.) I'm delighted to say that at Pitt, we needn't look further than our own students for inspired leadership. Life and death issues face us, and there's much work ahead for those of us who have pledged to consecrate our lives to humanity. In March, Matthew and James were granted an audience with the governor—a credit to their passion, positivism, adroit organizing, and leadership. If relief comes, these two second-year students will have had no small part.

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

Devoted to noteworthy happenings at the medical school ... To stay abreast of school news day by day, see www.health.pitt.edu.

At the Heart of the Disease

Fats accumulate on artery walls and harden into plaque—that's coronary artery disease. Immune cells then infiltrate the plaque, which explains why inflammation levels are elevated in patients with the disease. That's the traditional view. But which came first—the chicken or the egg? Accumulating research suggests that inflammation facilitates the buildup of fats on artery walls. Researchers at Pitt and other sites involved in the Women's Ischemia Syndrome Evaluation study have shed new light on this question. They measured levels of SAA, a protein that indicates inflammation, in women with chest pain and found that women who had higher SAA levels also experienced a higher incidence of heart attack, other cardiovascular events, and coronary artery disease. Though the data cannot prove which came first—the inflammation or the plaque—the strength of the link suggests that inflammation may play a role in the development of the disease, says Oscar Marroquin, assistant professor of medicine who is a coinvestigator in the study. ***—Dottie Horn***

FOOTNOTE

For all those who think that Scope and Scalpel is a frivolous diversion for medical students at Pitt: The great neuropathologist Santiago Ramón y Cajal said, "Of all men, physicians and playwrights alone possess the rare privilege of charging money for the pain they inflict on us." Apparently, Scope and Scalpel is good practice.

AMERICANS IN PARIS, INSERM IN PITTSBURGH

When one of the world's leading stem cell researchers, Frenchman Bruno Péault, broke the news to his boss, Christian Bréchot, that he'd been recruited to the University of Pittsburgh, he was surprised to find the news was met with enthusiasm. From the perspective of Bréchot, CEO of the French Institute of Health and Medical Research (INSERM), he wasn't losing a scientist, he was potentially gaining an international collaboration. Bréchot knew the Pittsburgh community well. Péault is now on the faculty at Children's Hospital of Pittsburgh and a professor of pediatrics and of cell biology and physiology at Pitt; he continues to be actively involved with an INSERM research unit. And he'll soon lead the first joint research unit between INSERM and a U.S. medical school; that unit will focus on stem cell research. Pitt and INSERM are also considering collaborations in psychiatry, transplantation immunology, hepatology, and computational biology. ***—Erica Lloyd***

CAMI MESA

A&Q

with Alik Widge on Politics—Gotta Have the Do Re Mi

Ask Alik Widge (shown above) for an interview, and be forewarned, this MD/PhD student has a question for you: Are *you* politically active? Widge currently holds the only spot for a medical student on the board of AMPAC, the political action committee of the American Medical Association. Since 1989, the bipartisan AMPAC has given nearly $20 million in contributions to political candidates and parties, making it one of the top 10 PACs in the country in terms of amount of money distributed, according to the Center for Responsive Politics. As a board member, Widge works to increase medical student involvement in the PAC and votes on each individual allocation of AMPAC funds. So far, he has completed two years at the University of Pittsburgh School of Medicine and is now in his third year of working toward a PhD in robotics at Carnegie Mellon University. This C-SPAN devotee aspires to hold political office one day.

On political involvement and cold, hard cash

You can have [a political candidate] who is the most ethical, brilliant person in the world, but they can't get elected unless they have [money] ... In 2002, the average House campaign was $898,000. ... What that means is that it's no longer enough just to go out and exercise your vote. If you are seriously going to be a citizen and participate in the process, you're also going to have to contribute to financially supporting candidates who are going to do the right thing for the patients of America.

On his perception of how politically interested medical students are around the country

That depends on how cynical I'm feeling on the day you ask me, honestly. There are days when I say, "Oh my God, nobody's interested. Everybody's just so bloody apathetic." ... There are other days when I feel really motivated and positive, and it's, "Oh, we've just got to talk to them, and they'll understand."

His question for the world

What are the issues that [our readers] really care about in terms of government, and who, of all the candidates out there, best reflects their views on that issue? If that candidate really does reflect their views on that issue, shouldn't they be doing something to help that person get elected? Can you really afford not to be [involved] if it's something you genuinely care about? ***—Interview by Dottie Horn***

Faculty Snapshots

A new finding by **Robert Bowser**, a PhD associate professor of pathology, may lead to faster and easier diagnosis of patients with amyotrophic lateral sclerosis (ALS), a fatal disease that causes progressive degeneration of motor neurons. People with ALS gradually lose the ability to move and often to speak, although their cognitive function is, in many cases, unaffected. Currently, the disease is diagnosed only when all other possibilities have been eliminated, a process that can take months. Bowser has identified differences in the cerebrospinal fluid of patients with ALS that allow him to distinguish ALS patients from controls. Bowser's finding may lead not only to a diagnostic test for the disease, but also to new targets for drug development. Last year, Bowser received the Chancellor's Distinguished Public Service Award for his work as director of Pitt's ALS tissue bank and his service to local ALS patients.

Bowser

Within six hours of the onset of symptoms, stroke patients might be treated with the clot-busting drug known as TPA. After six hours, it's believed that the risks of using TPA outweigh the potential benefits. (If used too late, the drug can cause life-threatening brain hemorrhaging and swelling.) However, **Tudor Jovin**, an MD assistant professor of neurology and VA investigator, believes there is a better way to decide who receives TPA. Jovin studied 36 patients with blockage of the middle cerebral artery who all had xenon-enhanced CT scans within six hours of stroke onset. The scan quantifies how much of the brain is already dead and how much is threatened but potentially salvageable. Jovin discovered that the severity of the consequences of the blocked blood vessel varied from patient to patient regardless of how much time had passed since symptom onset. "Some patients at five or six hours had less ischemia—tissue dysfunction and damage from lack of blood flow—than other patients at two or three hours," says Jovin. His study suggests that analyzing xenon CT scans, or using imaging technology that provides similar information, may be the best method for determining who should receive TPA. His study was published in the October issue of *Stroke*.

Jovin

Thirty thousand term and near-term newborns each year develop a potentially life-threatening condition called hypoxic respiratory failure, in which the lungs cannot supply sufficient oxygen to the body. Recent research by **Derek Angus**, an MD professor of critical care medicine, demonstrated the cost-effectiveness of treating these infants with inhaled nitric oxide. The study was published in the December 8 issue of *Pediatrics*. *—DH*

Immunosuppressives: Less is More and None is Best

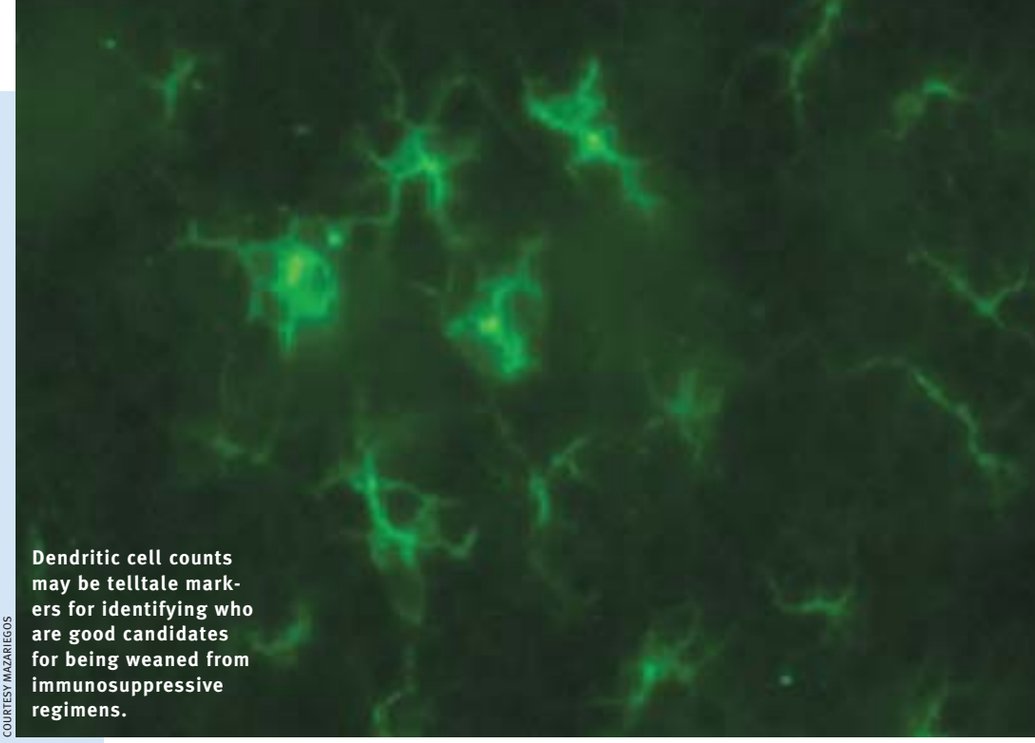
Fifty long-term survivors of liver transplants at the University of Pittsburgh are now completely free of immunosuppressive drugs—but that's less than 1 percent of the patients who have received liver transplants here. George Mazariegos, an MD associate professor of surgery, and other Pitt surgeons are working to make the percentage much higher.

Organ recipients typically receive steroids and an immunosuppressive drug; then, months after the transplant, doctors attempt to wean the patient off the steroids. At Pitt, since 2001, transplant surgeons have been using a steroid-free regimen whenever possible. Instead of steroids, patients are given an antibody treatment shortly before transplantation that weakens the immune system of the recipient without affecting the immune cells found in the donor organ. Following the transplant, patients are given lower-than-normal doses of an immunosuppressive drug. The hope is that the combination of antibody treatment and lower immunosuppression will allow the donor immune cells to gain a foothold and to establish a state of mutual tolerance with the recipient's immune cells—so that eventually the organ will be tolerated with little or no immunosuppression.

In adults who receive the steroid-free regimen and are doing well post-transplant, surgeons will try to wean the patient off immunosuppressive drugs three to six months following transplant. While not everyone can be successfully weaned, many patients are able to reduce the amount of drug they take.

Mazariegos is now trying to find blood markers that would enable physicians to distinguish which transplant recipients are good candidates for weaning. In a recent *American Journal of Transplantation* paper, he reported that increased type 2 dendritic cell counts seem to be linked to successful weaning.

Such findings may encourage other transplant centers to attempt to reduce immunosuppression. "One of the limitations that has discouraged other people from considering aggressive attempts at drug withdrawal is that it requires a lot of close follow-up," says Mazariegos. Pitt is currently the only center in the country that tries to wean patients from immunosuppressive drugs. *—DH*



COURTESY MAZARIEGOS

Dendritic cell counts may be telltale markers for identifying who are good candidates for being weaned from immunosuppressive regimens.

Inside a Tumor

Gliomas can be deadly brain tumors. Even with treatment, glioblastomas—the most common type of glioma—are usually fatal within a year of diagnosis. One strategy for fighting them is to develop drugs that inhibit the growth of new blood vessels that are necessary for the tumor to expand.

Last summer, Daniel Geynisman (Class of '06) studied gliomas while working in the shared lab of Kevin Walter and Eleanor Carson-Walter, who are both assistant professors of neurosurgery. The student showed that the plasmalemmal vesicle protein 1 (pv1) is more prevalent in the lining of blood vessels within gliomas than in normal brain blood vessel linings. The finding suggests that inhibiting pv1 could be a way to help stop new blood vessel growth.

Geynisman's work was supported by an American Brain Tumor Association fellowship; at the end of last summer, the association recognized him with the Lucien J. Rubinstein Memorial Award for completing the best research project among the fellowship winners. Besides kudos, he received $1,000. *—DH*

STROKES OF GENIUS

A new painting hangs in the lobby of the Biomedical Science Tower, showing Julius Youngner surrounded by the viruses that have compelled him to pursue his life's work. Youngner, now Distinguished Service Professor of Molecular Genetics and Biochemistry, worked with Jonas Salk from 1949 to 1955 as part of the Pitt team that created the killed polio virus vaccine. Youngner developed trypsinization, a cell culture technique now used in labs throughout the world, which made creation of the vaccine possible. Later in his career, Youngner unraveled mysteries of interferon and helped develop the FluAvert vaccine for horses. As artist Greg Kavalec created the portrait, the scientist posed for dozens of photographs, including close-ups of his eyes, clothes, and hands. "It's nice to see it hung while I'm still alive," he says.

—Dottie Horn and Sonya Kanti Patel

PORTRAITS PITTSBURGH/GREG KAVALEC

This portrait of Youngner now hangs on campus.

Balaban is working on a project with DaimlerChrysler that could keep drivers alert.

TOM ALTANY

Smart Seats

Sit in a prototype chair in Pitt's Augmented Human Performance Lab, and it feels no different than any other chair. But inside, in the seat and back, are 256 pressure sensors, spaced an inch apart, which take five readings per second. A computer records and processes the information. If you slump, fidget, lean, or shift your weight, the chair knows.

Eventually, the military may use this technology. Imagine a navy technician on a ship. She sits and watches a radar screen. Every time something new appears on her screen, she has to respond. Carey Balaban, who's developing the chair, envisions a seat that would monitor what the technician's posture reveals about her level of alertness and attention to the task. He's now testing the prototype to see if postural movements recorded by the sensors actually correlate with level of engagement in a task. Preliminary results suggest they do. In future studies, the PhD professor of otolaryngology will look at body movement and engagement in test subjects who sit in a prototype mounted on a moving platform that will simulate the motion onboard a ship.

His project is a Defense Advanced Research Projects Agency undertaking, but the technology has plenty of nondefense applications. Already, Balaban is working with DaimlerChrysler. He recently traveled to Germany to install a prototype chair in an experimental Mercedes-Benz sedan. The chair could become a safety feature in future cars. For example, drivers typically lean or shift their weight as they make a turn. If Balaban's pressure sensors don't pick up the appropriate body tilts as a driver turns, it could mean drowsiness or distraction, and a computer in the car could then intervene—perhaps with a verbal warning. Someday, the technology might even be used to help prevent long-distance truck drivers from becoming inattentive or from falling asleep at the wheel. *—DH*

Appointments

Twenty million Americans now suffer from asthma. The incidence of the disease has doubled in the past 20 years. The medical community cannot definitively explain the reason for the increase. Some blame environmental pollutants. Others have found evidence to support the "hygiene hypothesis," which posits that the decreasing rates of infectious disease in developed countries may skew the immune system in a way that makes people more susceptible to asthma. Research by **Lawrence Kane**, who recently came to Pitt as an assistant professor of immunology, may help shed light on why asthma is on the rise. Kane researches Tim1, a little-studied molecule found on the surfaces of immune, and perhaps other, cells. Other research groups, using a mouse model, have found evidence that suggests Tim1 is linked to asthma. Kane joined the faculty last year after completing his postdoc at the University of California, San Francisco.

Kane

In the January issue of *Nature Immunology*, **Binfeng Lu**, assistant professor of immunology, reported on experiments in which he halted function of the Gadd45-beta gene in the T cells of mice. "We demonstrated that the gene is very important for the function of T cells and in their protective [action] against infection," says Lu, who recently came to Pitt via Yale University. Better understanding of the gene and its effects could help researchers design strategies to boost immunity, says Lu. *—SKP*

Lu

ON THE TRAIL OF A DREAM

PROGRAM FOSTERS WOMEN LEADERS

BY KRISTIN OHLSON

CAMI MESA

ELAM alumnae at Pitt include (from left) Carolyn Meltzer, Katherine Shear, Kathleen McIntyre-Seltman, Jill Siegfried, Katherine Wisner. Not shown: Ann Thompson.

Tina had a feeling of disbelief about her husband's death, though he had died four years earlier. She often experienced a reverie state, in which she remembered being with him. At other times, she avoided going places that would bring up memories of him. Although she had seen a counselor, she had not responded to traditional depression treatment.

After working with patients like Tina (a composite of cases), Katherine Shear, a University of Pittsburgh MD professor of psychiatry, developed a vision. She had already created a specialized therapy for patients who suffered from this kind of traumatic grief. She began thinking that she should create a center in the medical school to study grief, develop treatments, and train practitioners—the type of center that doesn't exist anywhere in the country.

Yet she wasn't sure where to begin. Then Shear was selected as one of 45 fellows in the prestigious Hedwig van Ameringen Executive Leadership in Academic Medicine (ELAM) Program for Women, sponsored by Drexel University in Philadelphia. Established in 1995, the program is designed to increase the number of women in leadership positions in medical and dental schools. Each fellow participates in eight months of networking, mentoring, leadership training, and skill building—and develops a project on her home campus during the fellowship. Three weeklong sessions bring the 45 ELAM fellows together as a group. Each week is intense, with many small group exercises and seminars.

For Shear, ELAM's benchmarking exercise—commonly used in corporate America—was especially helpful. The summer before ELAM, she gave questionnaires on her work performance to her supervisor, peers, and those who report to her. During her first ELAM week, she met with a counselor to review information compiled from the questionnaires. Together, they identified her strengths and weaknesses, and Shear made plans to capitalize on a strength she hadn't previously used and to compensate for a weakness. She found that people thought she was creative and a great problem solver. She was surprised to see how highly everyone rated her (a common reaction among ELAM fellows). "Women tend to rate themselves lower than other people rate us," she says. "It's a dangerous thing to do, to underestimate your own strengths." Women also tend to remain less visible than their male peers in academia, so ELAM asks its fellows to meet with influential people at their schools. In Shear's case, she met with the dean, associate deans, and chief legal officer.

Shear is the sixth faculty member from the School of Medicine to participate in ELAM. Other Pitt fellows have launched projects ranging from raising awareness of lung cancer to developing training programs.

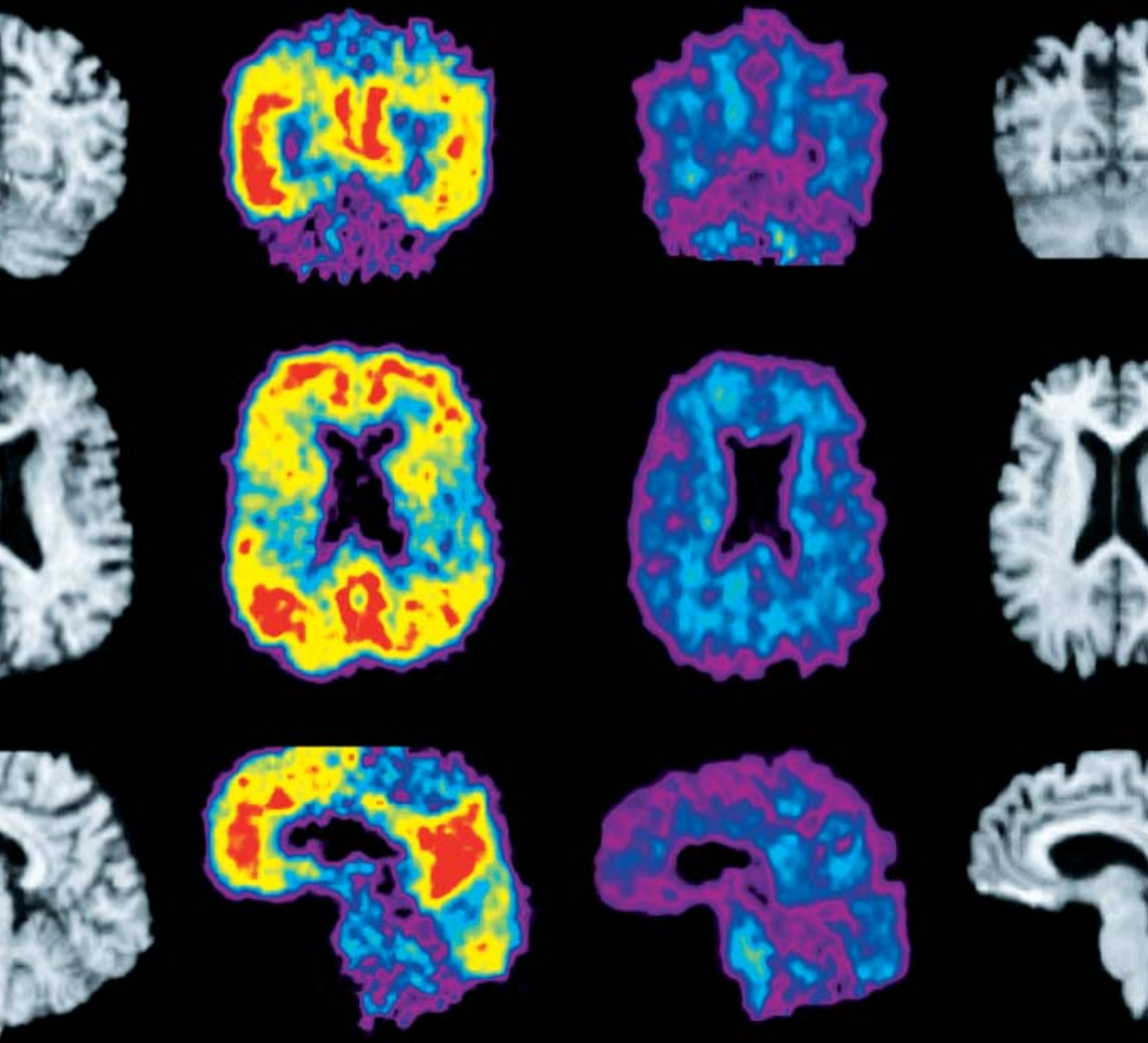
Now, as her fellowship draws to a close, Shear is well on her way to achieving the grief center, which became her ELAM project. She's identifying personnel for the center and has submitted two grant proposals.

"My plans for organizing the center have become much more concrete," Shear says. "I have more ideas for who to involve and how to involve them. Without ELAM, I don't think I would … have had the same vision for the center." ■

FOOTNOTE

Researchers at Oxford University have identified a rare "foreign accent syndrome" in people who have suffered brain injuries or strokes. In 1941, the first case was reported in a Norwegian woman who suffered a shrapnel injury to the head, leaving her with a German accent. We'll let yinz know if a Pittsburgh accent turns up in any unusual places n'at.

Explorations and revelations taking place at the medical school



For the first time, amyloid plaque can be detected in the brains of living people with Alzheimer's disease—using PET scans of patients injected with Pittsburgh Compound B (PIB), which binds to the plaque. The PET scan on the left shows an Alzheimer's patient with red and yellow areas of PIB accumulation, while the scan on the right, of a normal control, shows no PIB buildup. The difference cannot be detected in MRIs from an Alzheimer's patient (outer left) and normal control (outer right).

SEEING ALZHEIMER'S

COMPOUND MAKES THE DISEASE VISIBLE IN LIVING PATIENTS

BY KRISTIN OHLSON

In the early 1900s, a German neuropathologist named Alois Alzheimer began to work with a patient in her early 50s who had both cognitive and behavioral aberrations. After she died, Alzheimer examined her brain tissue and found gooey clumps of protein among her nerve cells. It was a momentous discovery, suggesting that the woman's mental disorder might have a physical cause.

In the decades since, autopsy after autopsy has revealed the same gooey clumps—now called amyloid plaque—in the brains of patients with Alzheimer's disease. Researchers have been able to find the plaque easily enough by applying various dyes to postmortem brain tissue samples. But in living patients, no one has been able to tell whether a person has plaque or to identify any physiologic evidence of the disease.

Until now, that is. In January, scientists at the University of Pittsburgh School of Medicine and at Uppsala University in Sweden announced that they had successfully detected plaque in living patients using a new compound—dubbed Pittsburgh Compound B (PIB)—in combination with positron emission tomography (PET). The discovery, published in the *Annals of Neurology*, offers a huge boost to Alzheimer's research everywhere.

In particular, the compound will prove to be a powerful asset to pharmaceutical companies attempting to develop antiplaque drugs for Alzheimer's patients.

"People have been working on these drugs for a long time, but it has been hard to know if they're effective when you can't see the target of the drugs in a living person," says William Klunk, an MD/PhD associate professor of psychiatry at Pitt and codeveloper of PIB.

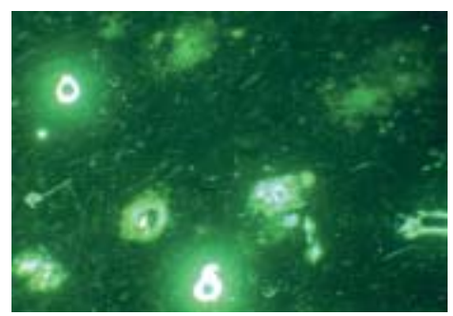
"It's like trying to develop drugs for hypertension without being able to measure blood pressure. You could just wait for the subject to have a stroke, but that's not a very good solution."

The new compound will allow researchers to diagnose Alzheimer's disease, track the growth of plaque in patients, and see if the new antiplaque drugs are actually having the desired effect.

For the last 15 years, Klunk has searched for a compound that could be used to flag plaque in living patients. Eight years ago, he teamed up with Chester Mathis, a PhD professor of radiology at the medical school. Mathis specializes in developing radiopharmaceuticals—compounds that are injected into the body and temporarily emit radioactive particles that can be captured by PET imaging to reveal anatomical clues.

Working with three classes of dyes used to detect plaque in the lab, Klunk and Mathis tested hundreds of compounds in both in vivo and in vitro studies. They needed a compound that could be safely injected into humans, that would penetrate the protective barrier that keeps most substances from entering the brain, and that would bind to plaque in the brains of diseased patients, while quickly clearing out of nondamaged areas of the brain. When they finally arrived at an effective compound, Klunk and Mathis arranged for human trials in Sweden, while waiting for approval of studies in the United States. They worked with 16 patients who were thought to have mild Alzheimer's disease, based on their clinical history, and nine patients in a healthy control group. Forty minutes after they were injected, the Alzheimer's patients as a group showed more than twice the amount of PET signal than the average in the control group. The strong signal was a result of plaque binding to the PIB, notes Mathis. The distribution of the signal corresponded well to that seen during autopsies of other Alzheimer's patients.

Three of the 16 displayed lower signals—about the same level as the control group. "When we rechecked the histories of these three, they were all atypical," says Mathis. "Their cognitive impairment was very mild, and they hadn't gotten any worse in two to four years. The implication is that they have some other form of dementia."



Postmortem tissue from an Alzheimer's patient shows amyloid plaque and rings of amyloid around blood vessels.

Klunk and Mathis will soon begin a trial in the United States of 100 healthy elderly people, injecting them with PIB and then doing PET imaging to detect plaque deposits. In those over the age of 75, the odds are about 25 percent of finding some plaque. The researchers will follow up on the participants who test positive to study the progression of the disease. ■

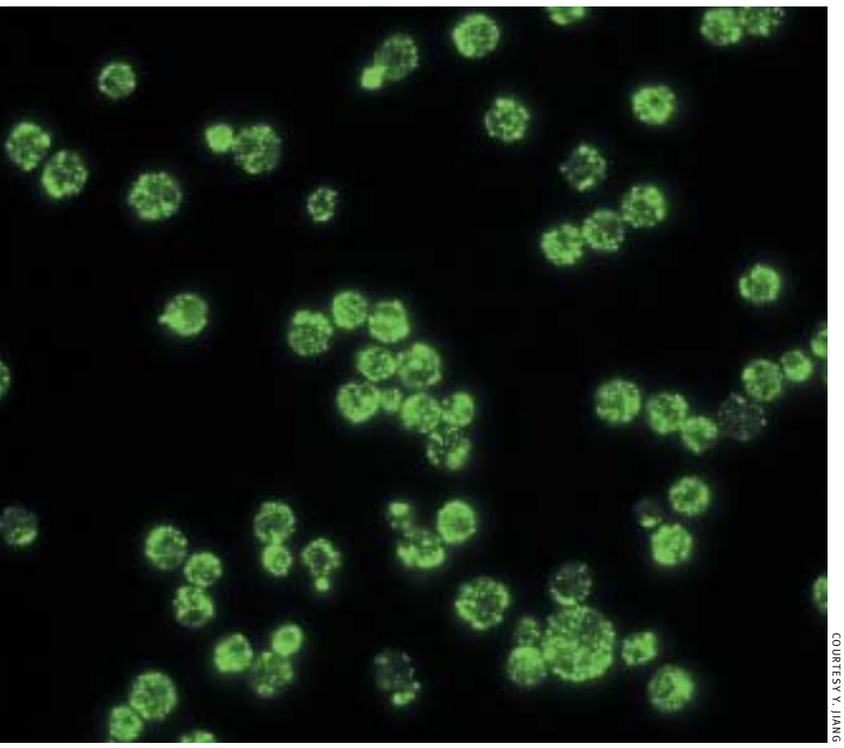
COURTESY C. MATHIS & W. KLUNK

RAPAMYCIN MOONLIGHTS

WHAT MAKES AN IMMUNOSUPPRESSANT A POTENTIALLY EXCELLENT CANCER DRUG? | BY ROBIN MEJIA

Sometimes a drug ends up being effective in a role its developers never would have expected. Rapamycin may soon prove to be such a drug. Now being tested in phase II clinical trials against breast and kidney cancer, rapamycin was originally approved as an immunosuppressant—it has been used in kidney transplants for several years.

Rapamycin's potential new role came as something of a surprise. Cancer patients need to boost their immune systems, so immune suppressors don't generally moonlight as cancer fighters. But it turns out that some tumors are strangely sensitive to the drug. At a dosage so low the rest of the body hardly registers it, rapamycin will stop tumors in their tracks. But studies suggest that only about 50 percent of tumors will be sensitive to the drug. How rapamycin works, and why it will arrest one tumor but not another of the same type, have become hot questions.



COURTESY Y. JIANG

In these yeast cells, a defective Tor pathway has resulted in abnormal distribution of the protein actin (labeled green). Actin is involved in cell growth; these yeast cells are not growing normally. Yu Jiang studies how the Tor pathway signals cell growth and how the drug rapamycin interacts with the pathway to curtail growth.

These are questions that intrigue Yu Jiang, assistant professor of pharmacology in the University of Pittsburgh School of Medicine. Jiang studies the Tor pathway, a sequence of molecular actions (rather like a complicated relay) that tells cells when and how much to grow and divide—the very functions that go into overdrive in tumors. It's also one of those nearly universal pathways that reminds us of our connections to the rest of the animal kingdom; apparently, this cascade of actions has been conserved throughout evolution. In just about all organisms, from yeast to humans, the Tor pathway seems to serve as a sensor of nutrient availability, limiting growth in times of starvation.

Researchers have learned that rapamycin targets the Tor pathway in cancer cells. It's as though the drug makes the tumor think that no nutrients are available—so the tumor stops growing. But scientists don't know all the steps involved in the pathway. Nor do they know how rapamycin brings about the arrested growth of the tumor.

Jiang came to the study of Tor during a postdoctoral fellowship at Princeton. At the time, his research actually focused on protein phosphatases (there are several types), which are important in controlling cell growth. As a postdoctoral fellow, Jiang established that protein phosphatase 2A was part of the Tor cascade. Recently, Jiang published research showing that by inhibiting Tor action, rapamycin also incites protein phosphatase activity. When the phosphatase activity stops, so does cell growth.

But the "million-dollar question," says Jiang, is how does activating phosphatases stop cell growth? It's a question he'll address in future studies. To learn more about how rapamycin works, he'll also pursue genetic studies in yeast. One by one, he'll "knock out" different components of the Tor pathway, to see if the yeast cells become more or less sensitive to rapamycin.

Jiang is optimistic about the possibilities for the drug. None of the chemotherapy drugs administered to patients today acts through the Tor pathway. And unlike many of these drugs, rapamycin has few side effects. Perhaps rapamycin could be used in combination with other chemotherapeutics, allowing them to be used in lower doses. Or it may even be effective as a stand-alone treatment. "Maybe your immune system will kick in and kill the cancer cells," says Jiang. Wouldn't that be a twist for a drug also used to repress the immune system? ■

THE BIG CHILL

BUYING TIME TO SAVE LIVES

BY DOTTIE HORN

CORBIS

A man is rushed in an ambulance to the hospital; he is bleeding internally from a deep stab wound to the chest. His heart is no longer getting enough blood to pump normally. As the sirens wail, the man's heartbeat becomes slower and slower. Just as the ambulance reaches the hospital, his heart stops.

Within five minutes, his brain will almost certainly be damaged. The trauma team starts delivering blood through an IV. Within 30 seconds, they've made an incision, spread apart the ribs, and gained access to the chest cavity. The doctors directly compress the heart. They look for an obvious bleeding site—perhaps a hole in the heart or in the lung—that they can quickly clamp or stitch. They see whether the loose sac that surrounds the heart has filled with blood and might be drained to give the heart the space it needs to work. Maybe there is a problem they can quickly fix. Usually there isn't. Eighty-five percent of the time, a patient in this situation dies. For all the efforts of the emergency department, he is likely to bleed to death, notes Samuel Tisherman, associate professor of surgery and critical care medicine.

But Tisherman and Patrick Kochanek, professor of critical care medicine and director of the Safar Center for Resuscitation Research, aspire to change this reality with an extraordinary new therapeutic strategy. Imagine again the stabbed man whose heart has stopped—doctors open the chest, but the steps they take don't help, and there's no quick problem they can fix. So, the doctors shift gears. They put a catheter into the aorta and flush ice-cold fluid through his blood vessels, until they chill the body to 50–60 degrees Fahrenheit. The cold temperature, they believe, will have a preserving effect, so that cells and tissues and organs will not be damaged even though there is no blood flowing through the body. The goal is to buy time—time to take the patient to the OR to locate and repair bleeding sites. Then doctors would begin circulating blood again. The blood would slowly warm the body, until it is warm enough to restart the heart, which typically will not beat below 86 degrees Fahrenheit.

This approach was inspired by earlier work by Ronald Bellamy, of the Walter Reed Army Medical Center, and the late Peter Safar, Distinguished Service Professor of Resuscitation Medicine. They imagined putting wounded soldiers in danger of bleeding to death in "suspended animation" to give them time to be transported to a hospital.

Tisherman and his collaborators have experimented with this procedure in anesthetized animals. To simulate a traumatic injury, researchers bleed the animal, cut open its abdomen, injure the spleen, and then stop its heart. For two minutes, no blood flows through the body; then researchers cut open the animal's chest and begin the cooling flush. After the approximate time it would take to get a patient to the OR, they remove the spleen. Animals can remain chilled with no blood flow for up to two hours and be successfully resuscitated—with no apparent damage to the brain. (The researchers test the animal's cognitive abilities after the experiment.)

Already, a similar procedure is the standard of care for some cardiac surgeries. Say a section of the major artery that carries blood to the brain is diseased and needs to be replaced with an artificial segment. For some replacement procedures, surgeons must cease all blood flow. To protect the body, they cool patients to 60 degrees Fahrenheit before the operation. The surgery is fatal 10 to 15 percent of the time. But in patients under 75 who survive, most are able to tolerate no blood flow for 30 to 60 minutes, apparently without cognitive or neurologic complications. (The extent of complications associated with this procedure has not been studied extensively.)

Tisherman and his group hope to begin clinical trials soon. But where will they find a pool of willing volunteers? Human research normally requires that participants sign an informed consent form, acknowledging that they understand and agree to an experiment. But, when doctors have only minutes to save the life of someone who is unconscious, it is impossible to obtain informed consent from the patient or a family member. A special provision, which allows researchers to obtain an "exception from informed consent," makes such clinical trials possible.

To be considered for an exception, Tisherman will have to consult with the community. First, he'll inform the community—through advertising or other publicity outlets—about the proposed research. Next, he'll explain the study to a group of community representatives; in deciding whether or not to approve the research protocol, the University's Institutional Review Board considers the group's reactions to the proposed research. Tisherman will also hold a public forum to allow anyone interested to learn about the study, ask questions, and comment.

So far, Pitt's review board has approved six protocols involving the exception from informed consent. One of those studies is being led by Clifton Callaway, assistant professor of emergency medicine; Callaway studies the effectiveness of having paramedics administer the drug vasopressin in cardiac arrest cases.

"We have to weigh the fact that [subjects] didn't give permission to be in this research against the fact that our current technology for treating this disease does not produce many survivors," says Callaway. "If we don't do this type of work, then we are frozen, and we will never be able to provide better care down the road." ■

IN SEARCH OF EARTHLY EXPLANATIONS FOR EATING DISORDERS | BY CHUCK STARESINIC

REFUSING SUSTENANCE

Catherine Benincasa was a rebellious child, strong-willed and stubborn like her mother, with whom she had a close but contentious relationship. The mother was a confirmed atheist, yet the daughter was somehow filled with religious devotion, even as a small child. At age 7, walking back to her home in Siena, Italy, from a visit with her older sister, Catherine reported a vision in which Christ held out a ring to her.

As she grew, Catherine wanted her mother to understand—or at the very least acknowledge—her profound belief in God, but the mother refused. The defiant adolescent strove to make penance out of the activities of daily life, even depriving herself of food against her mother's wishes. Unbeknownst to her family, Catherine began secretly throwing meat under the table.

Eating disorders are thought of as uniquely modern phenomena. So how do we explain Catherine of Siena, who presented symptoms of anorexia nervosa?

PAINTING | LINDA WALLEN

© CLEVELAND MUSEUM OF ART: PANEL FROM *ST. CATHERINE OF SIENA AND THE BEGGAR*, BY GIOVANNI DI PAOLO, CIRCA 1460

Catherine of Siena had no experience with fad diets or fashion models in *Vogue*. What did she have in common with those who suffer from eating disorders today?

When Catherine was 15, her sister, with whom she was very close, died in childbirth. Catherine should marry the widower, her mother insisted. He was a rich painter, and his wealth would ensure the financial security of the entire family. Already traumatized by the death of her sister, Catherine was being pushed to abandon her decision to devote herself to God. She fought back against her mother by entering into a prolonged period of fasting, which caused her to lose such a shocking amount of weight that her parents worried she would die. They desperately sought the intervention of the local priest.

The priest thought she must be saintly, stubborn, or insane, but he couldn't decide which it was. Eventually, after she gained admittance to a convent, her refusal to eat was trumpeted as a triumph of spirit over flesh. Self-starvation was a sacrifice so profound it indicated spiritual transcendence. (With no earthly explanation, her condition must be divine.) Catherine herself believed that God did not intend for her to desire food. Her sustenance was of a higher form. She severely limited her food intake for much of her adult life, sometimes taking food into her mouth to appease others and spitting it out at the first opportunity. She would sometimes use a goose feather to trigger regurgitation. She died after falling ill at the age of 33, undernourished and frail.

More than 600 years after her death, she is known as Saint Catherine of Siena. She isn't alone in the pantheon of saints—scores of Italian medieval saints also appear to have had symptoms of anorexia nervosa. Saint Theresa of Avila used olive twigs to induce vomiting, emptying her stomach before taking the Eucharist.

Eating disorders are frequently thought of as uniquely modern phenomena. So how do we explain Catherine of Siena and others who similarly suffered through the ages? In 1695, an English physician named Richard Morton described anorexic behavior in young women, as did Georgio Baglivi a few years later at the University of Rome. Sir William Gull coined the term anorexia nervosa in 1874. Catherine's contemporaries attributed her condition to the divine, as did she. But today, we insist on rational explanations for the human condition. We favor the physiological, biochemical, and neurological over the supernatural. Yet eating disorders have defied many of our best attempts at understanding. We point to the victim's environment, specifically indicting the family and Western culture. But Catherine of Siena had no experience with fad diets or the fashion models in *Vogue* magazine. What did she have in common with those who suffer from eating disorders today?

In psychiatric residency programs, they say you either like working on eating disorders or you don't. Once exposed, nobody is ambivalent. Walter Kaye was hooked from the start.

When he was a research fellow at the National Institute of Mental Health (NIMH) in the late 1970s, Kaye was asked to complete a study on anorexia nervosa. He became intrigued by the homogeneity of the disease—so many patients seemed to have the same symptoms. In schizophrenia and depression, by comparison, symptoms were all over the map. Anorexia seemed to be an area ripe for research, but funding and scientific interest in biological causes were limited, perhaps because the condition was believed to be self-imposed and culturally driven.

Kaye found that he enjoyed working with patients who suffered from eating disorders, too. They had a lot of similarities, beyond their obvious symptoms. For the most part, they were smart, decent, accomplished young people. It's true that there was a lot of mortality, more than in any other psychiatric condition, but many patients with eating disorders recovered and went on to do very well in life.

Gradually, it dawned on Kaye, who is now a professor of psychiatry at the University of Pittsburgh's Western Psychiatric Institute and

Clinic (WPIC), that there was something else that he saw in these patients who tended to be perfectionist, obsessive, and meticulous. "I have those traits myself," he says now, smiling like someone who long ago came to terms with his own idiosyncrasies. "I think a lot of researchers do. These are traits that can be very beneficial in certain professions, like engineering and medical research. And if you're not a little obsessional and perfectionistic in research, then you're not going to be very successful."

Researchers were beginning to believe that the similarities among patients with eating disorders were more than coincidental. In 1996, Kaye embarked on a landmark study—the first ever genetic study of eating disorders. Supported by the Price Foundation, he collaborated with centers all over the world to collect data on families with two or more cases of eating disorders. The primary goal was to see what set these families apart genetically from those without a history of eating disorders.

Important findings trickled out of the study. Kaye and colleagues showed that around 20 percent of fathers of anorexic patients had obsessive, perfectionist traits—very high compared to the general population. One might say this points to family environment as a causal factor, but it points to genetics as well. Women with bulimia were found to have altered levels of the mood-regulating neurotransmitter serotonin, even after they recovered from the eating disorder. Could this biological susceptibility explain why some women developed eating disorders when exposed to cultural influences and others did not? The serotonin re-uptake inhibitor Prozac was later found to help patients recovering from anorexia to maintain body weight, strengthening the notion that eating disorders were true biochemical imbalances.

Kaye says that he couldn't do the genetic studies without the contributions of Bernie Devlin, a Pitt PhD associate professor of psychiatry and human genetics. The two bring vastly different skills and personalities to their work. Kaye is soft-spoken and subdued, while Devlin is outgoing and animated. Kaye is an expert in the clinical presentation of eating disorders. Devlin is a statistical geneticist; he crunches numbers, and he crunches nucleotides. When Kaye first came to see him, Devlin could tell that the psychiatrist had been rigorous in gathering data. He recalls that Kaye said, "We have about 100 behavioral covariables we've assessed on these eating-disordered individuals, but we don't know how to use them efficiently in a genetic analysis. Do you?"

In other words, Kaye and his team had come up with a hundred different characteristics to look for in study subjects with eating disorders (more than 90 percent of whom were women). Was there a history of depression in the family? A history of obsessive behavior? Was this a purely restrictive anorexic patient (who restricts food intake but does not binge and purge)? Or does she binge and purge? Or purge during bouts of intensive exercise? Or display ritual behavior with food? Food obsession? Perfectionism? Kaye's team had compiled the most detailed record ever made of patients with eating disorders—a mountain of data which, according to Devlin, "they knew in their hearts and minds would be useful, but they didn't exactly know how to use."

Devlin says he and his team spent "a year or two" working out the methodology for analyzing this wealth of data. The job required experts in the genetic basis of behavioral characteristics, experts in genetic analysis, and experts in statistical analysis.

In the 1990s, geneticists were beginning to rack up an extensive list of diseases linked to specific genes. They were filled with confidence that if a disease had a genetic component, that component could be uncovered. With the sequencing of the human genome, geneticists became even more confident of future successes.

Scores of Italian medieval saints also appear to have had symptoms of anorexia nervosa.

But when Devlin ran data on eating disorders, he came up with lemons. His lab took 192 families with various eating disorders and processed the data. The links were weak, at best. Then they began using some of Kaye's 100 behavioral covariables as filters. When they separated out the families in which at least two relatives had restricting anorexia nervosa—characterized by severe limitation of food and no bingeing or purging—the results clearly pointed to a region of chromosome 1. When they looked at bulimia—characterized by bingeing and purging—the results pointed to chromosome 10.

Their methods may shed light on other complex illnesses. After sequencing the human genome, geneticists around the world have been searching for new ways to mine the data for keys to disease. It's becoming more and more clear that many diseases with genetic components aren't like cystic fibrosis or hemophilia, in the sense that they won't be linked to a single mutation. Devlin calls these "simple genetic diseases," and he does not count eating disorders among them.

"The recognition that complex diseases were going to be so hard to crack really only came within the last decade," he notes. When asked to explain why, he quips, "Optimism," and laughs. With eating disorders, the underlying genetics can't be linked to a single gene, or even to one region of the genome. Many genes are involved, and the linkage signals are much weaker, he explains. "The patterns are more difficult to see. You can't find these chunks of DNA nearly as easily, and even when you do it's not so clear what genetic variants in that region are responsible for the expression of liability to the disease."

Devlin says that partly as a result of their study, geneticists have been eager to apply similar methods, i.e., using a large number of secondary characteristics to unravel complex genetic diseases, but most researchers are finding they simply don't have data as detailed as what Kaye and his colleagues have been gathering since the mid-1990s.

Based on their promising results, Devlin and Kaye have won support from the NIMH for a $10 million study of the genetics of anorexia nervosa—the first government-funded study of the genetics of anorexia nervosa. They hope to enlist 400 families with two or more cases of anorexia, a considerable challenge, but one that they expect will lead to more significant discoveries. Nine clinical centers around the world will join with WPIC to recruit families and gather data over the next five years.

Kaye recognizes that it may take a long time for public perception of eating disorders to change. There's a deeply ingrained attitude that if anorexics weren't exposed to images of shockingly thin super models they might cease being so "stubborn" and begin to eat more. While those images may contribute to the disease, the soft-spoken psychiatrist quietly challenges the facile nature of the assumption that they're the primary culprit: "Anorexia has the highest death rate of any psychiatric illness. Ten to 15 percent of these people will die. People don't starve themselves to death because of purely cultural influences. *You* try to starve yourself to death. *You* eat only 200 calories a day for a couple of months. How do you think you'd feel? There's a powerful physiological drive to eat. There's something wrong with that physiologic drive in anorexia."

We once believed that schizophrenia was caused primarily by environment, Kaye points out. Now, it is accepted that culture and family play a role, "but if you don't have certain susceptibilities," the psychiatrist says, "it's not likely that you will develop the illness. The same thing is true of anorexia. It's just that we're 20 years behind in relation to other major psychiatric problems."

At the Eating Disorders Clinic at WPIC, the beds don't stay empty for long and neither do the maroon-upholstered chairs in the common room. The furniture is blocky and square, institutional but warm. There are usually several patients curled up in the chairs, reading or talking. Almost always, they are young women.

The dry-erase board behind the front desk lists about 15 patients. Dates of admittance show that one has been present for over a month, though most have been here for two to four weeks. Today, all are designated "201," meaning they are here voluntarily. Sometimes, a code will change to 302, meaning that person tried to check out against medical advice and is now here involuntarily, usually a minor being treated with parental consent.

Some patients come from a long way off, including parts of Ohio, where the entire state is without inpatient treatment for eating disorders. Maria LaVia, the medical director of the clinic and attending physician for inpatients, says that treatment options for eating disorders have decreased around the country as centers have closed or cut back their programs. Managed care has pushed for less hospitalization and shorter stays across the board. Plus, many insurance companies now limit coverage for what they term "chronic mental illnesses." Some explicitly cover all mental illnesses except eating disorders.

This clinic offers outpatient services, too, including a partial hospitalization program, where patients come five days a week, eat their meals, and go home in the evening. There's an intensive outpatient program where patients come three evenings a week to eat dinner and have group, individual, or family therapy. This high volume of patients makes WPIC a good place to conduct research. LaVia, who is collaborating with Kaye and Devlin, hopes that many of the 400 families recruited for the NIMH study will come from this clinic.

But the patients don't come here for genetic research. This clinic is where the rubber meets the road—where the long arm of chromosome 10 doesn't mean much of anything to a high school senior who weighs only 75 percent of her ideal body weight and is mortally afraid of gaining another pound. This clinic is where the gold standard is weight gain, not genetic analysis.

LaVia says they are finding treatments that work, many tailored to the specific diagnoses and the subcharacteristics of each eating disorder. Prozac and other drugs that work on the serotonin system are helping bulimics. There's the promise of similar drug therapies for anorexics in the near future. Family therapy has been shown to help anorexics younger than 18. Cognitive-behavioral therapy—learning to understand your own behavior and embrace alternatives—is helping bulimics. The program is evidence based, so all of these approaches have been proven effective to some extent in the scientific literature. Methodologies supported by anecdotal evidence or having theoretical benefits, like the 12-step programs used at some centers, are not employed here.

"People don't starve themselves to death because of purely cultural influences. *You* try to starve yourself to death."

The treatments for eating disorders address what we know about the disease—biochemistry, neurotransmitters, behavior, family environment, self-image, culture. These are not likely to change. Genetic makeup will never morph into determinism, nor will it fully exonerate cultural triggers like rail-thin models, fad diets, and the objectification of women. So how does genetic research change things for those struggling with eating disorders?

So far, hardly at all, says LaVia. "I think in general people have a hard time wrapping their minds around the fact that psychiatric illnesses are not all environmental. The theory was always this: If you are depressed, you just need to pull yourself up by the bootstraps, and get yourself out there, and cheer yourself up, and get on with life."

But acceptance of a more biological paradigm could go a long way toward removing the stigma associated with eating disorders.

"Patients often blame themselves," says LaVia, "because they've caused this illness themselves by not eating, or by eating and throwing up." She would love to see more patients identify with the analogy of, for example, a diabetic woman, who certainly did not choose to stop controlling her own insulin. She feels the same about parents who, at the end of their rope, ask their child, "Why can't you just get over this?"

Gazing into the distant future, LaVia imagines a day when she might examine a patient, diagnose a specific eating disorder, and then order a genetic test to confirm the diagnosis—sort of like diagnosing an infection and confirming it with lab work. Such tests might help psychiatrists convince and enlist the help of parents who resist the diagnosis. "I can't tell you how many families come in and say to me, 'My daughter does not have an eating disorder,'" says LaVia.

She likes this notion that elements of psychiatry might begin to resemble other medical specialties. (Then, perhaps, fewer people would be surprised when she informs them that, yes, psychiatrists also went to medical school.) LaVia thinks this would benefit patients, too, as they struggle with managed care.

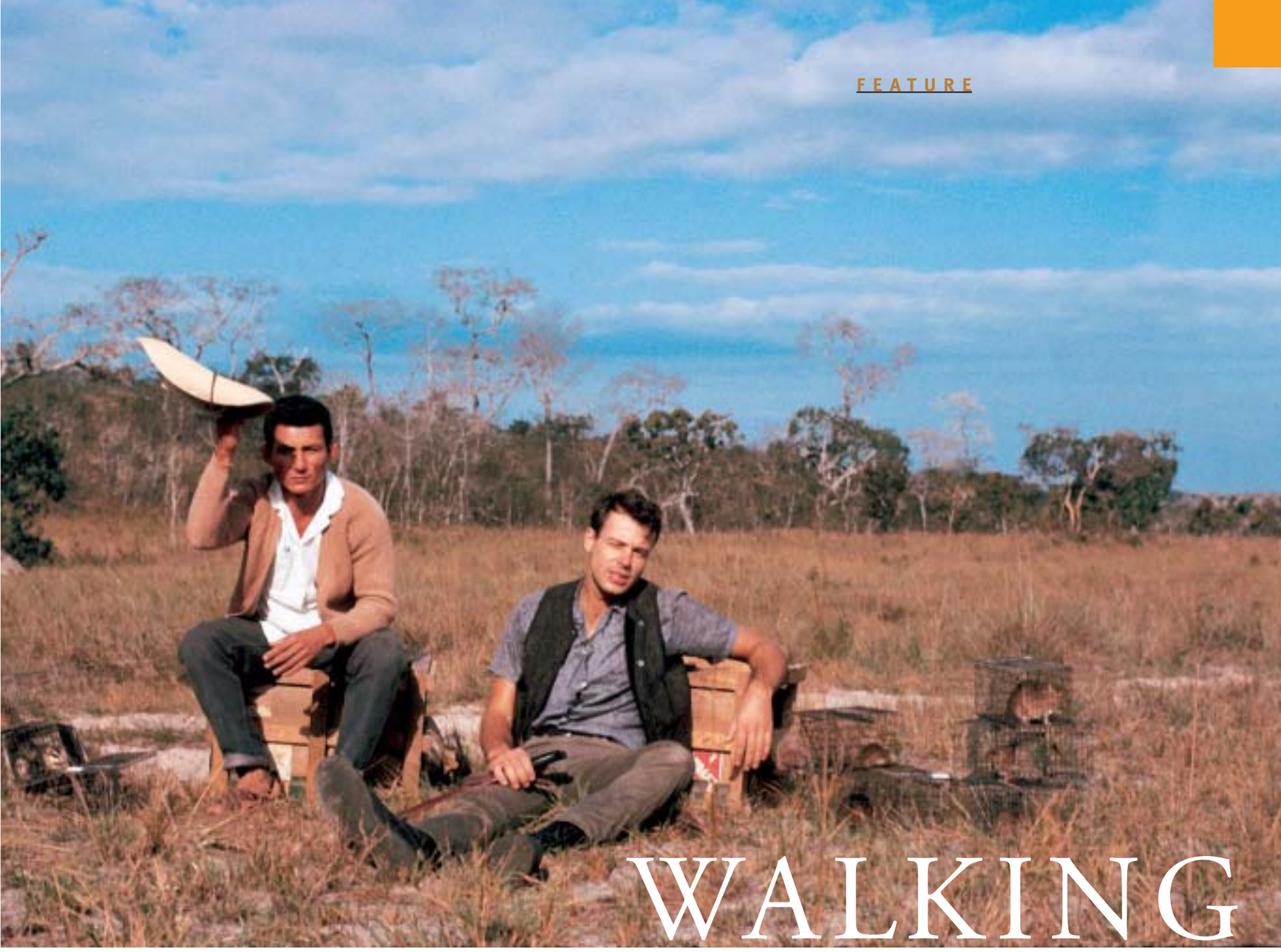
"I keep getting back to insurance," she says by way of apology, "but from a clinical standpoint it's a huge obstacle. In psychiatry in general there are limits to your insurance coverage. Per calendar year you may get 30 days of inpatient coverage, and you often get 26 outpatient visits. And I try to think of other medical illnesses: Would an insurance company say, 'You can only be in the hospital for 30 days this year for your diabetes, and if you need to be in the hospital more than that, you're going to have to pay for it out-of-pocket'? You know, that sounds crazy."

Like her colleague Kaye, LaVia finds eating disorders especially poignant partly because of the demographic they tend to afflict—90 to 95 percent are women in their teens or early 20s who are often trying to get an education and make important decisions. For physicians, who know what it's like to work hard under pressure, it's difficult not to identify with these patients and want to help them, says LaVia.

"They can go from being very good, very high-achieving kids to being kids who can't do as much because their illness is interfering with their ability to either attend school or to continue in the path they had originally hoped to follow." ■

To take part in the genetic study of anorexia nervosa in families:1-888-895-3886
www.angenetics.org

COURTESY HIBBS



WALKING BEFORE DAWN

HOW A KNOWN POLLUTANT BECAME THE NEXT BIG THING

BY ERICA LLOYD

It's not clear how they got lost, but the air commandos who were transporting the research team had been drinking the night before. They were somewhere over the billion-acre Amazon rain forest, and the C-46 was running out of gas.

John Hibbs Jr. (right) in Bolivia in 1964 on an animal trapping quest to find the source of a mysterious and deadly virus. He is sitting with Einar Dorado, a colleague who contracted the virus and died.

COURTESY HIBBS

Hibbs (center) and others from the Middle America Research Unit testing animals to learn how far the virus had spread.

Captain John Hibbs Jr. (MD '62) and the others put on their parachutes. It didn't look good. At least Hibbs had a pistol and a survival kit—a few fishing hooks, matches, a knife, and scarce few other necessities in a waterproof package put together for him by his kid brother. Jimmy had given him the kit as he was preparing for this assignment with the U.S. Special Forces (Airborne). As it turned out, Hibbs didn't have to rely on the foresight of his 14-year-old brother back home in Pennsylvania to get him through. That day in 1964, the crew managed to figure out where they were with the help of the sun and the sextant. More important, they were able to land safely.

Hibbs had finished his internship at the University of Oregon when drafted into the army; while serving with the special forces in Panama, he volunteered to help the Middle America Research Unit investigate an outbreak of hemorrhagic fever centered around San Joaquin, Bolivia. The fever was killing 60 percent of the people who'd contracted it. Hibbs' mobile field research lab was sent into the surreal landscape of the Paraguayan Chaco and into the Brazilian Amazon to trap and tag animals to decipher the source of the infection and how far it had spread. Their charge covered a vast wilderness comparable to the land mass stretching from the Mississippi to the Pacific. There, Hibbs was treated to plenty of made-for-movie characters—from hung-over commandos to Indians running in rivers to catch piranhas for dinner. All part of the job. Hibbs expected the assignment would bring adventure, something that had always called to him. What he hadn't expected was the intellectual ride microbe hunting would prove to be. His best finding was discovering that science was "true high adventure," as he says. Under the direction of Karl Johnson, the team discovered that mice from Bolivia and the chaco carried persistent Machupo virus infection, the cause of the fever. In the middle of the last century, expanding human settlements and climate cycles had brought the mice, notably their feces and urine, into contact with human food.

As an undergraduate at Dartmouth College, Hibbs majored in history. He later enrolled as a medical student at the University of Pittsburgh, where his father, John Hibbs Sr. (MD '34), a scholarly internist in the Uniontown area, had also gone to school. (As a boy in Uniontown, Hibbs Jr. had to walk through his father's waiting room to get to the family living quarters upstairs.) At Pitt, he was bowled over by the caliber of the faculty. Hibbs studied pathology under department chair Frank Dixon and his faculty—"Many of them were founders of modern immunology," he notes. Hibbs soaked up their enthusiasm for understanding the mechanisms of disease. Likewise, Klaus Hofmann and his group made chemistry come alive. Despite his admiration for Dixon and Hofmann, the wings of Scaife Hall where basic science investigation was pursued seemed like foreign territory.

"When you're learning—mastering—knowledge that already exists," notes Hibbs, "it's a very different thing than trying to learn something new about nature."

Since his time in the South American wilds, Hibbs has learned about the joys of, he says with a broad smile, "carrying on a dialogue with nature." When he talks about his work, it's as though this fit 67-year-old is speaking about a secret club, and he can't wait for you to join. Learning details of the world around him is a high. As a child, he loved spending days with his grandfather, who had a farm in the mountains near his family's rural Pennsylvania home. Maybe he would be a farmer, too, the boy thought for a while. His grandfather taught him the name of every plant in the countryside; Hibbs has done the same for his three children. Despite his thrill-seeking inclinations, there's little bravado in Hibbs' gentle demeanor. He lives in Utah now, and his voice echoes the evenness of a western plain, of a boy who once dreamt of plows and sweet-smelling earth. One colleague described him as a meticulous hound dog when it comes to his research, reticent to publish findings until he has thoroughly fleshed out the ambiguities. (The same care and attention is afforded to his patients at Salt Lake City's veterans and university hospitals; the house staff recognized Hibbs with the Outstanding Teacher Award four times.)

Among other important advances, Hibbs' decades of assiduous give-and-take with the natural world have helped to unravel an entirely new principle for signaling in biological systems and the human body. In 1977, pharmacologist Ferid Murad reported that coronary arteries opened in the presence of nitric oxide; he theorized that the body might actually release the gas. But conventional wisdom at the time said nitric oxide was a byproduct of auto exhaust, a pollutant, not something our bodies would generate. Meanwhile, Hibbs, completely independently and in a totally different field, immunology of infectious diseases, was unknowingly putting puzzle pieces in place that would prove Murad was right.

There's some irony in nitric oxide's intellectual history. Inventor Alfred Nobel suffered from heart disease and then died after a stroke in 1896. Despite his doctor's urging, he'd refused to take nitroglycerin—an explosive he thought he knew well because it was a key component to his invention of dynamite.

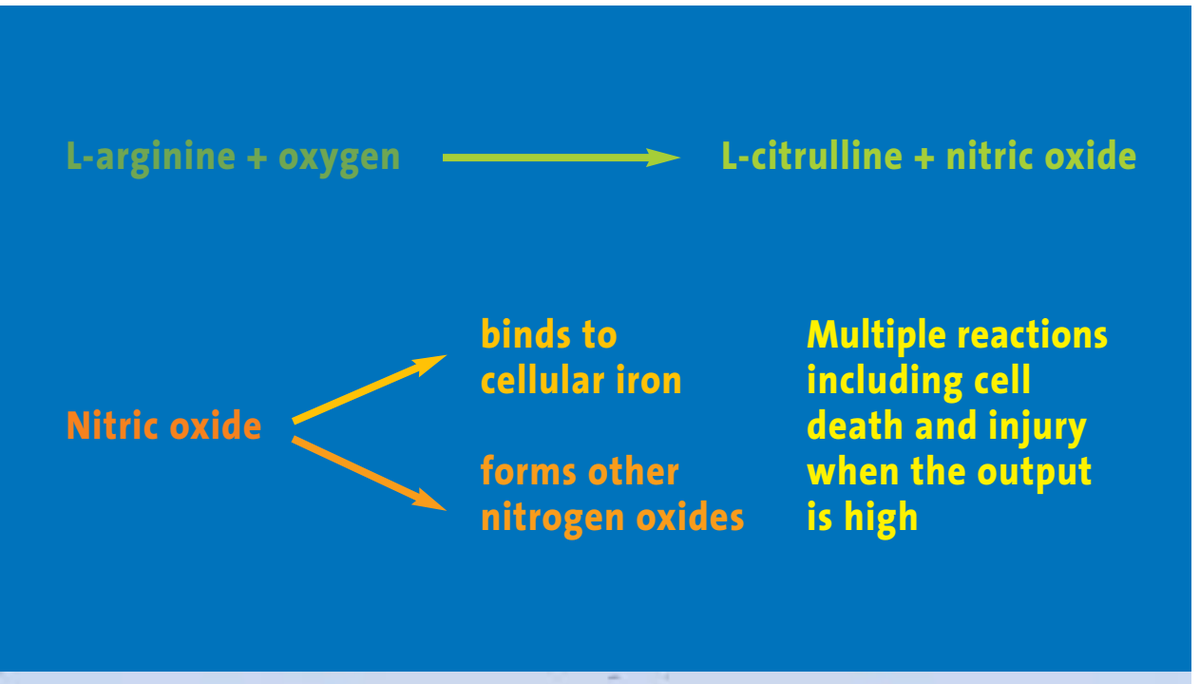
COURTESY HIBBS

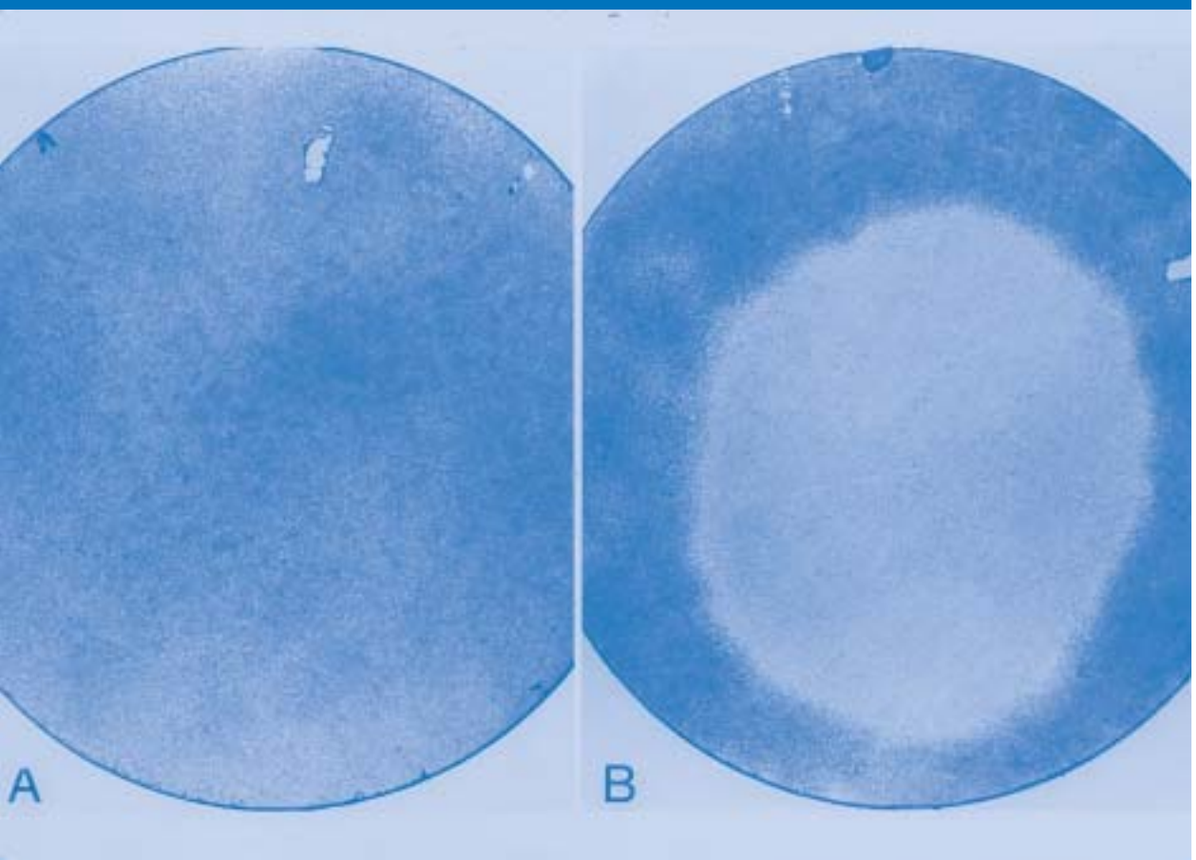
One-hundred-and-two years later, the Nobel Foundation, which Nobel had created from his considerable fortune, recognized Murad, Louis Ignarro, and Robert Furchgott with the Nobel Prize in Physiology or Medicine for their discoveries concerning nitric oxide as a signaling molecule in the cardiovascular system. Murad had revealed that the century-old treatment for chest pain, nitroglycerin, acts by releasing nitric oxide. From all accounts, that's the tip of the iceberg in terms of nitric oxide's power over biological systems.

Hibbs had never met anyone with so much passion. Anything Jack Remington focused his attention on—windsurfing, rock climbing, skiing, or immunology—he pursued with extraordinary gusto. Remington, an infectious diseases specialist at Stanford University and Hibbs' new adviser, seemed to have more energy than a Pacific gale; and that's a topic Hibbs would have known something about. After his service in the army, Hibbs had returned to Oregon for his residency, then set sail for 10 months in the Pacific as part of a crew of five on a 39-foot sloop on a 24,000-mile journey. On his return, the life of a scientist awaited him, and it proved just as invigorating. Hibbs thrived as a fellow under Remington.

Remington was exploring how our bodies fight intracellular microbes, pathogens that antibodies can't reach because they become protected by the cell membranes they invade. He had shown that mice infected by intracellular microbes experienced an immunity that was not specific to any one disease. In other words, if animals were infected with, say, the bacteria that causes tuberculosis, they developed a resistance not only to the very pathogens they'd been exposed to—*Mycobacterium tuberculosis*—but also to other intracellular pathogens, be they bacteria, viruses, or protozoa. The key to this resistance seemed to be the macrophage, the cellular scavenger in the linings of blood vessels and organs. Hibbs wondered if activated macrophages would work the same way with cancer—that is, if their ability to ward off a gamut of uninvited guests would extend to tumors. It did. When he placed macrophages from mice infected by intracellular microbes with tumor cells, the tumor cells either died or stopped growing. (The macrophages hardly affected normal cells.) And it didn't matter if the tumor cells were from mice, rats, or humans—the activated macrophages from mice still offered resistance.

(This is beginning to sound like a cure for cancer. In fact,





ABOVE LEFT: Who would have thought that nitric oxide, a known pollutant, played a key role in vascular health, immune response, behavior, inflammation, impotence, shock, cancer, memory, and then some? Hibbs delineated the biochemical pathway our bodies use to synthesize nitric oxide. BELOW LEFT: (A) No activated macrophages equals no cytoxicity. The dark area is covered with tumor cells growing normally. (B) Tumor cells don't grow in the white area, where they meet up with activated macrophages. Hibbs discovered this as a fellow in 1970. Determining how the macrophage managed this trick would keep him occupied for a good 16 years.

similar experimental techniques with intracellular microbes have been used effectively in certain melanomas, leukemias, and in a bladder cancer. Yet the approach has limited utility.)

But how did the macrophage provide resistance? What was the mechanism? Hibbs wouldn't be satisfied until he found out.

For the past 33 years, John Hibbs Jr. has maintained a research laboratory supported by the Department of Veterans Affairs and the National Institutes of Health; in addition, he is the chief of infectious diseases for the University of Utah. In 1999, that university recognized him with the title Distinguished Professor of Medicine. The machete he used in the Amazon is now a poker for the fireplace in his home set in wooded hills not far from canyoned wilderness; it's the same home in which he and his wife, Francoise, have resided since they moved to the Salt Lake City area in 1971 (they added on as their family grew). He and Francoise start their days at 5 a.m., hiking in the mountains near the university.

Hibbs expected the assignment would bring adventure, something that had always called to him. What he hadn't expected was the intellectual ride microbe hunting would prove to be.

There is an epitaph devoted to founders of Pitt's Allegheny Observatory that could be a theme for Hibbs' approach to life. It reads, "We have loved the stars too fondly to be fearful of the night." On Hibbs' epic 24,000-mile sail, he learned celestial navigation. The big test came when they were looking for Easter Island, which is only 50 square miles in size. Hibbs became sold on the ancient method when one morning he looked off the bow and—wow!—there was the island, on schedule and exactly where they'd predicted.

Hibbs loved the night shift at the helm. The sun's glare could be disorienting. But how could he not welcome nightfall when, as he puts it, "all of a sudden, the world is old friends and landmarks"?

He is quite comfortable making his way in the dark. His work for more than 30 years has been a gradual and steady progression of seminal observations that began at beaconing sites he first came across under Remington's tutelage. When he set up his own lab at Salt Lake, Hibbs was determined to probe this nonspecific resistance phenomenon more mechanistically. What was it that created the toxic response in tumor cells and microbes?

Another lab had repeated Hibbs' activated macrophage experiments but shown that macrophages from normal mice could kill tumor cells when infused with type 2 interferon. Hibbs saw for himself how well this worked with his bench experiments. Then, working with Brice Weinberg and Harold Chapman, fellows in his lab, he saw that almost every lab chemical they added to the serum with type 2 interferon ended up inciting the process and killing more tumor cells. Something was off. *Everything* couldn't be an immune activator. The investigators became suspicious that the commercially acquired supplies they'd been using were contaminated and took on the unpleasant task of visiting a slaughterhouse to collect blood themselves to use as serum. At a local slaughterhouse, they saw workers putting blood into stainless steel buckets, amid the bile and guts around them, wearing the same clothes they had worn as they performed all the other tasks required of them that day. Hibbs asked them what they were doing. Well, they were collecting blood for a commercial serum supplier. It struck Hibbs that these guys knew as much about sterile techniques as he knew about flying a 747 (nil). The scientists became convinced they were likely to find bacteria in the serum they'd been buying. They were right. It was full of endotoxin, a byproduct of bacteria. Every batch was loaded with the stuff. Then they tested other chemicals they'd been using; those contained endotoxin as well. When they removed the microbial products and tried the interferon experiments again, the macrophage wasn't nearly as potent. From there, Hibbs' lab demonstrated that type 2 interferon primed the macrophage, but the macrophage wasn't activated until it came into contact with microbial products. (The mice Hibbs had infected back in Remington's lab produced interferon as part of their immune response.)

This told the scientific world a couple of other important things as well: The results that labs everywhere had been reporting—across disciplines—could have been affected by the very serums and chemicals they'd used. Also, the macrophage deserved recognition as an extraordinarily sensitive immune sentinel. Macrophages were positioned throughout the body, ready to detect and act on the presence of microbes. And their response could be subtle or quite violent (as in the case of the contaminated serum and also septic shock, the biomedical community would learn later).

Hibbs poked and prodded further. He discovered that an analogue of the amino acid L-arginine inhibited the macrophage's ability to kill tumor cells. Further, L-arginine itself was absolutely essential for macrophages to be toxic to pathogens and tumor cells. Eventually, he pieced together the biochemical pathway that created the macrophage's toxic effects. He demonstrated that in an enzymatic reaction, L-arginine was somehow converted to citrulline (another amino acid). But at the time, an L-arginine-to-citrulline reaction was not understood to take place in the human body outside the urea cycle. And the reaction Hibbs saw was different from what happened with urea. There was another oddity: When Hibbs tracked the pathway, he couldn't account for where a nitrogen atom had gone. It seemed to have vanished from the equation.

In the meantime, biochemists at the Massachusetts Institute of Technology were interested in how nitrite-enriched foods affected the body. They were concerned that nitrite (the salt of nitric acid) was carcinogenic. MIT's Steven Tannenbaum had discovered that our bodies somehow synthesize nitrates (a similar salt). This seemed to happen only in the presence of microbes. When checking one study subject's urine, Tannenbaum noticed his nitrate levels had spiked. The subject happened to have a fever. This prompted Mike Marletta and Dennis Stuehr, astute young scientists in the same lab, to treat mouse macrophages in tissue culture with endotoxin, resulting in the production of nitrite and nitrate. They thought maybe the salts were a byproduct of inflammation. Hibbs read about these findings in January 1986.

That's when it all came together for him. Hibbs realized where the wayward nitrogen atom had gone, nearly ending a 15-year-long chase for the elusive mechanism that rendered the activated macrophage so potent. It made sense: a nitrogen oxide must be the missing biochemical link—responsible for

killing the tumor cells and Remington's intracellular pathogens. This conclusion was fortified by another finding. With the help of Donald Granger and Jean-Claude Drapier, inspired fellows in his lab, he'd learned that the activated macrophage had damaged tumor cell mitochondria, causing iron to leak out of the cells. Nitric oxide was known to perturb iron metabolism.

In July 1986, he submitted his findings to *Science*. They were published in January.

Scientific universes were colliding right about then. Independent of Hibbs and the MIT scientists, Louis Ignarro and Robert Furchgott had just concluded that nitric oxide was released in the cardiovascular system. Back in 1980, Furchgott had observed that smooth muscle cells in the cardiovascular system relaxed and dilated in the presence of an agent he called EDRF (endothelial derived relaxing factor); Ignarro and Furchgott independently reported their conclusions that EDRF was nitric oxide at a conference in July 1986, when Hibbs submitted his paper. Ignarro then collected more data supporting his hypothesis, which *Circulation Research* delayed publishing until December 1987, because the data seemed so unlikely. Hibbs showed soon after, in 1988, that nitric oxide, a highly unstable molecule that exists for less than 10 seconds before it's converted to the end products nitrite and nitrate, was indeed the molecule that macrophages used to kill tumors and microbial cells. Marletta reported at the same time his own unequivocal biochemical evidence that nitric oxide was produced biologically.

By then, interest in nitric oxide had exploded in the biomedical community. NO, the shorthand name for nitric oxide, was an overnight sensation. Tens of thousands of papers on the molecule have been written since Ignarro's and Furchgott's presentations. Who would have imagined that a gas—of all things, a known pollutant—passed through cell membranes to play the role of a vital metabolic regulator?

As it turned out, nitric oxide is produced by many cells in the body besides macrophages. We now understand, thanks first to Hibbs, that it's a weapon against infection. It's also a signaling molecule in the nervous system, a regulator of blood pressure, and a gatekeeper of blood flow. Nitric oxide helps us recognize different scents and appears to play a role in memory and behavior. It's considered key to developing better treatments for atherosclerosis, certain intensive care situations, cancer, and impotence (the gas is the magic behind Viagra). It plays a harmful role in sepsis and circulatory shock, so the development of NO-inhibiting treatments is regarded with great optimism. In fact, Pitt's Department of Surgery, a hotbed of NO investigation under chair Timothy Billiar, was the first to show that NO production increased in humans experiencing sepsis. (The department lays claim to many NO "firsts," including identifying and cloning the gene for iNOS, an enzyme that triggers production of nitric oxide in the body. Pitt's nitric oxide beginnings came in the late '80s when Billiar and then-chair of the surgery department, Dick Simmons, collaborated with one of Hibbs' inspirations, Klaus Hofmann.) Hibbs' own work as a NO pathfinder continues to this day.

Murad, in his Nobel lecture, noted Hibbs' contributions and that Hibbs had never been sufficiently recognized for his important observations.

"Many in the field, including myself," confides Billiar, "feel that John Hibbs' contributions to the discovery of the nitric oxide pathway were significant enough to warrant sharing the Nobel." He was nominated for the prize.

Each day, Hibbs walks before dawn, before the aspens play their games with light and shadows. At his office in the Veterans Affairs building, he works quietly, out of the spotlight. He hasn't published much in the last few years, notes Granger. But, "the best is yet to come," Granger is convinced. His old mentor is piecing together how our bodies adapt to stress metabolically—more on nitric oxide. "I think it's extraordinarily important work," says Granger. "The government should give him a *carte blanche* research grant. I can't think of anybody I'd put above him for scientific and humanistic honors."

Hibbs' current puzzle involves some of the most difficult biochemistry he has ever encountered, "sort of a Lewis Carroll–*Through the Looking Glass* chemistry," Hibbs says. A few years ago, he thought he would retire about now, but the biology he's trying to figure out has just begun to crystallize for him, a culmination of 15 years of effort. He'd like to see it through. "There's really something important there," he says. His grant money runs out this summer, however. And he's not sure that he'll get funding to continue. ■

COURTESY HIBBS

Hibbs on one of many family hikes. This was taken in Idaho; the Teton Range is in the background.

Jay Kolls and his team may soon run the table with a vaccine for pneumonia in AIDS patients and a stem cell therapy for cystic fibrosis. Kolls (left) and Chad Steele (background and right) don't get to play much pool lately because their research results are coming fast and furious.

BIG BREAKS MAY BE ON THE WAY

FOR APPROACHING DEADLY LUNG DISEASES

BY DAVID R. ELTZ

RACK 'EM UP

In the Big Easy in the late 1990s, if you worked in Jay Kolls' gene therapy lab, it helped if you shot pool. On any Wednesday after a day at the bench, Kolls would lead his researchers at Louisiana State University to a nearby pub for a debriefing. But you had to bring change. Kolls, with his deceptively boyish grin and giggle, was known for running the table all night without spending a quarter.

If the results from the LSU bench were coming fast, though, you'd find him in the lab well into the night, peering at petri dishes for the halo of a blooming virus or pondering the latest confocal microscopy images for the expression of a gene.

Even now, Kolls, a professor of pediatrics at the University of Pittsburgh since fall 2003, can as easily be found picking a classic rock tune on his Fender Stratocaster or wielding a pool cue as he can slipping on his white lab coat. And that smooth, natural transition between coolness and intensity has, for Kolls and his team, produced the perfect atmosphere for results.

PHOTOGRAPHY | CAMI MESA

He and his colleagues believe they have developed a potential vaccine for the pneumonia that kills children with AIDS, and they are likely to be the first to put bone marrow stem cells into patients with deadly cystic fibrosis.

Jay Kolls was born in 1959, the middle child of a nurse and a pediatrician. He grew up in the small town of Salisbury, Md., amidst the pungent aroma of the surrounding poultry farms.

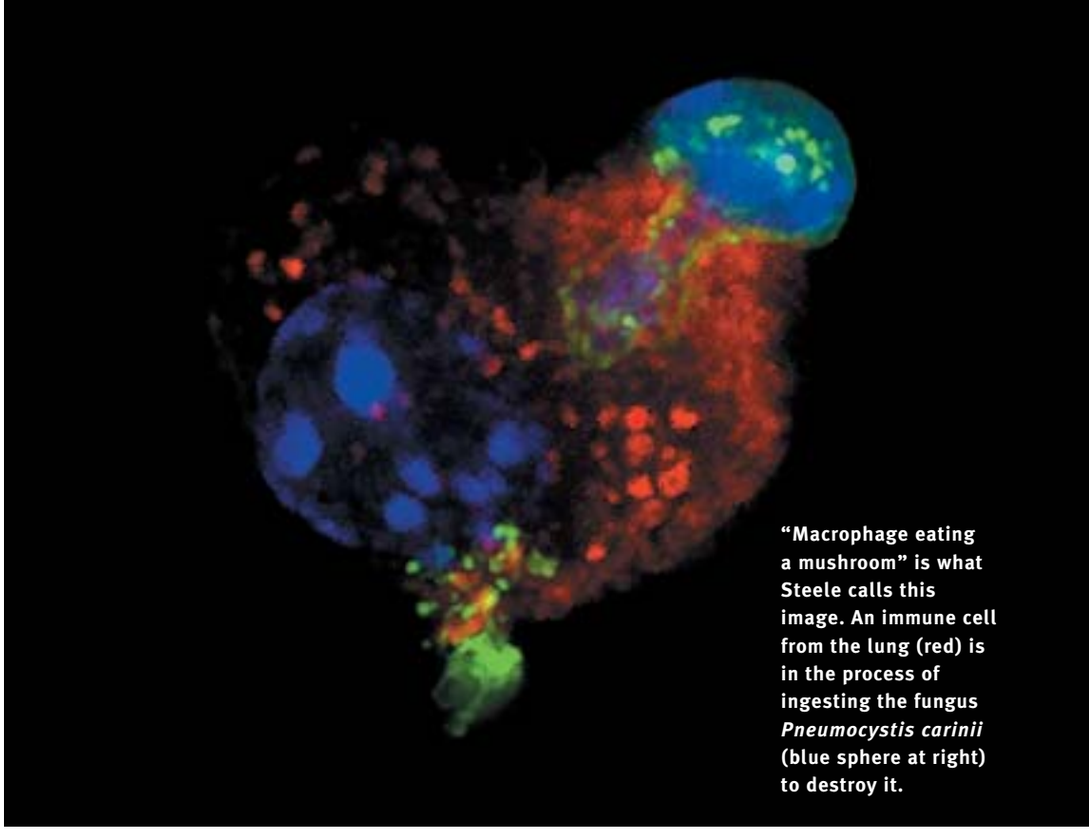
At Ursinus College, near Norristown, Pa., Kolls learned poker. (He still plays, but not well, reports one friend. He has too much fun drinking beer and laughing, says another, who still refuses to shoot pool with him.) Kolls majored in physics, liking its practicality and mathematical steadfastness.

He enrolled in medical school at the University of Maryland, where he struggled with the staid curriculum at first. *Here's the substrate. Here's the enzyme. Here's the product. Memorize it.* Finally, in clinical rotations, he felt he could be creative. At the Baltimore VA, Kolls heard of Warren Summer, a renowned pulmonologist and teacher. Summer had left Johns Hopkins to head a program at LSU, and Kolls arranged a senior elective with him at Charity Hospital in New Orleans.

Charity was a free hospital overloaded with inner-city patients, many in advanced stages of disease. There, Kolls saw one of the great urban scourges, tuberculosis. He saw mesothelioma, lung cancer caused by asbestos. (At the time, asbestos was used to insulate the hulls of ships built in New Orleans.) And Kolls saw one of the ravages of AIDS, the fungus *Pneumocystis carinii,* which causes a pneumonia.

Kolls landed an internship at LSU in pediatrics and medicine. One night, an AIDS patient suffered a respiratory arrest. Kolls and a nurse, Cynthia Cowart, intubated him. Three years later, they were married, still joking about meeting over a code.

By July 1989, Kolls had begun a dual fellowship in pediatric and adult pulmonology. He would spend the first of four years as a pediatric pulmonologist at nearby Tulane University, joining the adult pulmonology group at LSU in the second year. Kolls recalls that the gene for cystic fibrosis (CF) was discovered around then. "That was an exciting time; there was talk within minutes of the discovery of gene therapy," Kolls says. About the same time, a woman, 34, was hospitalized at Tulane. She'd previously been misdiagnosed with Wegener's granulomatosis, a rare disease of the respiratory tract. The woman had undergone heavy immunosuppression for a year, to no avail. Tests at Tulane revealed she had CF.



"Macrophage eating a mushroom" is what Steele calls this image. An immune cell from the lung (red) is in the process of ingesting the fungus *Pneumocystis carinii* (blue sphere at right) to destroy it.

The experience was a watershed moment for Kolls. In most people, the cilia attached to the epithelium in the lungs catch invading bacteria and drown the organisms in a pool of sodium chloride. In 30,000 young adults in the United States however, the cilia become impotent from fighting constant infection. Eventually, bacteria bore into the epithelium, causing chronic pulmonary problems that kill 90 percent of those with CF by a mean age of 31. Kolls was struck by the fact that symptoms of CF hadn't presented until she was 30, even though she'd obviously had the disease for years. He also was amazed that she could be immunosuppressed for so long without getting too sick. The immunology of lung disease held new fascination for him.

By 1991, Kolls headed for the bench, taking a spot in Judd Shellito's lab. Shellito had come to New Orleans from the University of California, San Francisco, having developed the first mouse model for pneumocystis pneumonia, the most common pediatric illness associated with AIDS and leukemia, particularly in sub-Saharan Africa. (About 90 percent of childhood HIV occurs in Africa; nearly 50 percent of those children will die from pneumocystis pneumonia, which is caused by the fungus *Pneumocystis carinii.*) The pneumonia occurs when a person's disease-fighting CD4 helper T cell count falls below 500. Along with a viral load test, a CD4 count is indicative of the extent of a patient's HIV infection.

Kolls became interested in a disease-fighting cytokine, tumor necrosis factor (TNF), which is produced by macrophages in response to infection. In diseases like arthritis and pneumonia, overproduction of TNF seemed to contribute to the disease. Summer, LSU's chair of pulmonology, helped Kolls win a prestigious Parker B. Francis Fellowship. Kolls moved to Dallas to work at the Howard Hughes Medical Institute in the lab of Bruce Beutler, who'd elucidated TNF's role in sepsis.

Beutler had made a transgenic mouse that weakly expressed an inhibitor of TNF. Kolls and Beutler talked about another approach: What if Kolls could make a virus that changed a mouse's genes, causing it to express the inhibitor? He started trying to make the virus in October 1992. By February, Kolls got the mixture of cells and agar, a translucent material that in a dish makes the glass look like a dirty window, just right. Ten days into culture, a telltale clearing, a halo of plaque, formed. He'd made his first virus. After another month of letting the virus grow, Kolls injected the substance into mice and challenged the mice with the bacterial disease listeria, which was thought to be dependent upon TNF. If the virus worked, the mice given the TNF inhibitor would be more susceptible to listeria. They were. In fact, his virus caused the mice to make so much TNF

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inhibitor, they died. The work proved that, as an alternative to knockout mice, you could use viral vectors to make what Kolls calls a "poor man's" transgenic mouse.

"This was really something that was quite an advance at the time," says Beutler, now a professor of internal medicine at the Scripps Research Institute in California. "The TNF gene hadn't been knocked out (in mice), and it wasn't really clear what a strong TNF blockade would do."

In July 1993, Kolls took a faculty appointment in medicine and pediatrics at LSU, continuing his work with Summer and Shellito. Summer recalls Kolls was so energized with new ideas and techniques that the pulmonology chair insisted each of LSU's lung grants have a transgenic component using Kolls' technology.

He became section chief of the pediatric pulmonology lab and director of the gene therapy program at LSU. He was also thinking about focusing his research on specific diseases. As a resident, he'd worked on pneumocystis in Shellito's lab; the disease, with its signature overproduction of TNF, and his technology seemed a perfect match. He started using his TNF receptor virus to inhibit various genes associated with the disease. But there were problems. "Everything I did made the infection worse," Kolls says. "I realized after a year that you can't go too far [in your career] by making infections worse."

Kolls was unsuccessful in getting his TNF receptor virus to help make infections better, so he switched gears. Eventually, he made two related viruses that *did* seem to work. In one ongoing project funded by the National Institutes of Health (NIH) since 1998, Kolls caused a mouse to produce interferon gamma, which helps macrophages make TNF. The interferon gamma caused T cells to change into cells that specifically helped fight lung infection. Kolls believes his virus technology caused macrophages to kill the fungus more effectively.

Another ongoing project might lead to a vaccine for pneumocystis. The CD4 helper T cell count of HIV-infected children is so depleted, they don't have an immune system strong enough to respond to a vaccine. In 1999, Kolls wondered: What if you worked around those cells? Other researchers had shown that you could genetically engineer dendritic cells in the bone marrow to tell the body to make antibody to fight infection.

Kolls discussed the idea with a postdoc, Mingquan Zheng. Zheng studied the technology and learned how to build dendritic cells from the bone marrow of mice with no CD4 cells. In the process, he engineered the cells with pneumocystis antigen, and gave the dendritic cells back to the mice—in effect, creating a cell-based vaccine using the mice's own cells. The mice developed the antibody to pneumocystis. The antibodies also offered protection in the long term; the team could challenge the mice again with pneumocystis, and they wouldn't develop infection. The researchers could even put the serum into other mice with no immune systems at all, and they too were protected against infection.

Kolls and his team set out to discover the critical antigens in pneumocystis that the mice were responding to. They've since identified two, cloned one, and left dendritic cells behind. Dendritic cell therapy, though considered a wave of the future, takes time and resources to create, meaning only the affluent will be able to afford such treatment. So Kolls' lab has been working, instead, with a DNA-based vaccine, which is much easier and less costly to grow. It's also a stable technology, not easily destroyed outside the lab. "You can ship it to Africa or wherever HIV is a major problem," Kolls says. Now he's vaccinating mice. Primate studies could be on the horizon. So might an application for investigational new drug status from the Food and Drug Administration to test efficacy in humans.

When Kolls came to Pitt in 2003, he took over pediatric pulmonology at Children's Hospital of Pittsburgh. Kolls also brought with him, from his New Orleans lab, Zheng, Chad Steele, Florencia McAllister, and Xue-Jun Zhao. Kolls sits in his office at the Rangos Research Center, still appearing boyish in his mid-40s, wearing a black polo shirt, talking about another potential blockbuster project he'll soon move to Pitt.

In the late 1990s, Kolls took note of research by others showing you could tease bone marrow stem cells to become bone culture in vitro. For about a decade, researchers had been trying to get viruses into the lungs of CF patients, only to fail because of natural barriers like cilia and sodium chloride that fight invaders. "This makes sense, evolutionarily," Kolls says. "You would not want your lung epithelium easily infected by viruses; we'd be sick all the time."

But what if you harvested a patient's own airway cells and grew them with bone marrow stem cells? Working with collaborators at LSU, Kolls' team took such cells from patients undergoing lung transplants, mixed them in culture with stem cells marked with a green fluorescent protein, and watched as the cells divided. After two weeks, they had green cells growing cilia that looked just like epithelial airway cells. What's more, before culture, the stem cells didn't express the CF gene. At the end of 14 days, they did. Work is still under way to determine if the CF gene in these new cells causes the secretion of sodium chloride, meaning the cells would be functional. So far, two experiments have shown they are functional.

Can the stem cells differentiate in a human? Kolls believes he will know soon. He's preparing for a study at Pitt in which a few patients with CF would give bone marrow samples. Kolls would extract stem cells, alter them with a normal CF gene for therapy delivery, grow them in culture, and then plant them back into the walls of patients' sinuses. (CF patients tend to have terrible sinus infections that often require surgery.) After a few months, Kolls would have them come back for a biopsy to see if the cells differentiate in the sinus wall just as they do in culture.

The FDA may ask Kolls to do animal studies to test for adverse effects. Kolls could get the technology classified as an investigational drug by September. With the FDA's blessing, he could go to the NIH to fund a clinical trial, starting in early 2005, just to see if the technology works. Then Kolls has to figure out how to deliver the therapy to the lung.

Remember the natural barriers—the cilia and sodium chloride—that protect the lung from invaders? Kolls' stem cell treatment would need safe passage around those guardians. There could be a way. When you get an infection in your lung, macrophages send signals called chemokines to attract homing molecules, which then bind to chemokine receptors on the macrophage. Kolls wonders if he can engineer the therapeutic stem cells to express these receptors. If so, maybe he could get the therapy to bind directly to macrophages and home to the lung—without getting trapped in cilia and drowning.

That would be like smacking all the solids on a pool table into separate pockets on the break. Then, again, Kolls has been known to run the table all night. ■

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MARX BROTHERS IN *A NIGHT AT THE OPERA* © BETTMANN/CORBIS

ALL TOGETHER NOW!

LAST IMPRESSIONS ARE EVERYTHING

BY MEGHAN HOLOHAN

Blue paint covers one side of Neil Badlani's face. Looking up, his dark eyes fierce, he raises a plastic battle axe in his hand and shouts, "They can make us disimpact until our fingers bleed!"

The crowd surrounding him roars in agreement. Guitar and keyboard riffs from the '80s rock anthem "Eye of the Tiger" reverberate in the background.

"They can make us learn textbooks full of useless information!"

Another shout from the crowd. Badlani, a third-year medical student at the University of Pittsburgh, wears a T-shirt, shorts, and plastic armor as he stands on the Cathedral of Learning lawn, inspiring a crowd of fellow medical students.

"They can leave us $300,000 in debt! But they WILL NEVER . . . TAKE . . . OUR . . . SCOPE AND SCALPEL!"

Cheers rise. The students start running away from the camera on the Cathedral lawn.

The TV screen fades to black.

A December storm has just dumped a half-foot of snow on the ground. North Oakland is eerily still. There are no cars on the roads; few are willing to brave the icy hills. Inside Josh Englert's apartment, about a dozen med students are sitting on couches, futons, and camping chairs, eating Chinese food and watching Badlani on the television. Badlani's performance as "Braveheart" was part of the video shown at the medical school's talent show a few weeks earlier. By showing this rerun, the writers set the mood for the first full script reading of Scope and Scalpel—the graduating class' annual show, during which the students parody Pitt med school. This will be the 50th anniversary of Scope and Scalpel. And this may be the first production ever to have a draft completed before winter break.

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(Standing, from left) Josh Englert, Brad Sobolewski, and Neil Badlani present the first full script reading for the 50th anniversary show.

Badlani, Englert, and Brad Sobolewski stand in front of their peers. They are the three head writers for this year's show. The three seem very different from one another, yet their differences helped to make the script one that works on many levels, without relying too much on sophomoric jokes. As Sobolewski notes, "Two songs about poop is two songs too many."

Englert is tall and lanky. He often rakes his hand through his brown hair. His humor is subtle and witty; it makes you think for a moment. He says he's obsessively organized. While writing, he taped little pieces of paper with ideas all over his folder—his way of organizing the flow of the story.

Badlani is gregarious; he has the timing that makes good comedy and comedic writing. His athletic frame looks comfortable as he lounges in editing sessions or when he dances around. He has stage presence. "We start with mental exercises, which is what we are doing now," he said during one writing workshop, closing his eyes a little, looking meditative, as Madonna's "Material Girl" played on a portable CD player and his collaborators watched him with puzzled expressions. When the leadership was trying to think of titles, Badlani named three in rapid succession: "*No Sex in this City*, *Bend over Like Beckham*, *Harry Clotter and the Chamber of Secretions.* It's *No Sex in this City,* and we'll tell people Sarah Jessica Parker is in it." (His collaborators groaned, and the show went for several more months without a title.) Badlani's quick wit was sharpened during his few stints as a stand-up comic in Washington, D.C.; that was while he was an undergraduate at George Washington University. "I don't really want to be a doctor; I really, actually, want to be an actor," he says. The enterprising Badlani spent last year earning an MBA at Pitt's Joseph M. Katz Graduate School of Business—to help him with administrative duties later in his career, among other reasons. Even though he's a third-year student, he wanted to lend his comedic talent to this year's class, the class he started med school with. Hence he found himself among the creators of the 50th anniversary show.

Sobolewski speaks in metaphors and bizarre juxtapositions—ideas for the show came to him like "nervous butterflies on drugs." He is generous, often referring to Englert's and Badlani's strengths. The Pittsburgh native, who uses "yinz" and says he has Allegheny River water running through his veins, jokes that he minored in interpretive dance while also studying biology at Washington & Jefferson College in Washington, Pa. A few years ago, Sobolewski performed in the medical school talent show in what was the only act of its kind. He picked "volunteer" and fellow student Dale King out of the audience and as music from *The Barber of Seville* played, danced around King, pretending to cut his hair. Then the music switched to the *A-Team* theme song, and Sobolewski shaved King's hair into a Mohawk. Next came the Mr. Clean jingle, when Sobolweski's dance approximated that of, as he describes it, a "caffeinated hummingbird." That's when he shaved King's head bald.

Sobolewski has been writing and editing in between interviewing for pediatric residencies—11 interviews in all.

Producers Jonathan Bickel and Rachel Norris sit in the corner of Englert's living room. Bickel has been involved, in some way, with Scope and Scalpel for the past four years. He is excited about the progress this class has made for the 50th anniversary production. Yet, he is nervous. Well maybe not nervous, apprehensive, and cautious. First there are the live monkeys. From the first day the leadership of Scope and Scalpel met, Badlani, Englert, and Sobolewski have been talking about using live monkeys in the show.

"We love monkeys," Badlani says on another winter day. "I can't promise monkeys, but I'm doing my best. We'll find room for the monkeys—they're an integral part of the show."

"There is no way we're getting live monkeys on the stage," Bickel confides later. "I'm the producer, and they're not getting monkeys on the stage. And no ponies either." (There must have been talk of ponies as well.)

When Bickel was in junior high school, a friend of his was attending a Pittsburgh acting school. Bickel asked his parents if he could participate, too. Since then, he has played

everything from Jesus in *Godspell* to a flamboyant King Charlemagne in *Pippin*. When he attended Earlham College in Richmond, Ind., he was the technical director of a radio variety show that was similar to Garrison Keillor's *A Prairie Home Companion*.

Bickel has been interviewing for pediatric residencies and, as part of a research rotation, researching PDA applications that will help doctors record medical information. He's devoting his time to this show because he has seen, as he puts it, some "pitfalls and mistakes" of the past years; he wanted to create a bigger and better show.

Animals aside, Bickel is focused on what needs to happen before March. There are a lot of ifs to consider. As he sees it, everything will work out *if*, by mid-March, the cast members are selected, and the set designers are drawing the sets, and everyone is gathering props, and the fundraising has gathered steam. Then the show will be stellar.

At this point, though, Bickel doesn't even know what the script will be like. He hasn't participated in the writers' meetings; he left the creative work up to Badlani, Englert, and Sobolewski. So he, like the other senior students in Englert's apartment, sits, waiting to hear if this script will be the funniest.

Upbeat music fills Englert's apartment—it's from *Annie*—and Badlani, Englert, and Sobolewski start belting out lyrics. Not the familiar lines from the lovable musical. Like Scope and Scalpel writers from the past, the trio has twisted the lyrics to reflect the med school life.

Sunny skies we never see
Sunny skies . . . no way . . . no sir-ree
No one cares for you a bit
Med student you ain't shhhhh

Badlani turns and shakes his rear end (a sight they'll see several times during the three-hour reading). He hops around facing the crowd, gyrating his hips (another soon-to-be familiar sight). When the music suddenly switches to rap, Sobolewski's blond head bobs as he pushes the air with his hand, like many rap stars do. People chuckle; Bickel's loud belly laugh often rises above the rest.

Englert, who isn't just obsessively organized, but is also a natural storyteller, recalls a scene from *Crouching Patient, Hidden Finger,* the Class of 2002's Scope and Scalpel. He describes a grandly choreographed dance of wheelchairs and walkers set in a Veterans Affairs unit; the cast sings its own corrupted version of Kenny Rogers' pop country hit "The Gambler." The number ends as a miniature American flag is hoisted from an IV pole.

That May night two years ago, as he wiped tears of laughter from his eyes, Englert knew that he had to write for his Scope and Scalpel.

Englert calls himself a rising fourth-year; others might just say he is on a leave of absence. Because he took this year off to do research on treatments for sepsis and shock in the lab of Mitchell Fink, who is chair of the Department of Critical Care Medicine, he's not technically in his fourth year of medical school. Englert is considering going into critical care medicine; he's drawn to both basic research and the clinical side. He thinks this research year has helped him to become more detail oriented and helped organize his thoughts for the show.

Early in the writing process, Englert dreamed that Badlani made him go to Scope and Scalpel. One problem: The script hadn't been written. In his dream, Englert was horrified to watch the show flounder. After that, it was a while before he stopped asking himself: *What did you get yourself into? Do you want this responsibility?*

"I do it for the glory; Neil is doing it for the girls—it's not working."

Scope and Scalpel has become each graduating class' legacy. In 1955, student Sam Aronson (MD '55) was talking to pathology chair Frank Dixon about how to bring the class together in their final year after clinical rotations. Then the idea was born—the fourth-year students should put on a show. The first production was named *PMS IV*. (As the ritual matured, so did the titles of the shows, including *Lost in Scaife, Cramalot, Tuition Impossible, Forrest's Lump,* and *Saving Ryan's Privates,* to name a few.) Ross Musgrave, alumnus (MD '43) and director emeritus of the Medical Alumni Association, was the faculty director of the first production. He challenged the Class of 1956 to carry on the tradition. That class staged another production, and Cyril Wecht (MD '56 and Allegheny County coroner) dubbed the theater society Scope and Scalpel.

Fifty years of students roasting their school, professors, deans, and medical center is a lot for these writers, directors, and producers to live up to. There have been years when people were shot out of cannons. There have been pyrotechnics. This year's Scope and Scalpel members are all acutely aware of the pressure that a golden anniversary brings. When the organizers first met, they agreed on some guidelines for the script and the production.

The first goal—make the production the best ever. Not a small task.

Each year, Scope and Scalpel is likely to have this debate: Should the script have an overarching storyline that connects all the skits? Or should the production be more of a variety show with the skits standing on their own? For this year's production, the leadership wanted a strong story to connect all the skits.

"We want to entertain and have a story. We want the audience to bond with the characters," says Badlani. "It's much more interesting this way, and there's more direct audience engagement."

Another goal—make sure the production wasn't full of inside jokes that only the class shares.

"It's nice to have the whole room laughing," coproducer Norris says. "Our goal was to make sure that everyone has a great time, which includes the audience and our parents. We want people who haven't been here for the past four years, but can appreciate the four years we've spent here, to laugh."

With all these considerations in mind, the writing was slow at times, Englert admits. Some scenes just fell together. One classmate wrote a song based on a tune from the musical *Chicago,* and the head writers easily constructed a scene around that song. Other scenes took a lot more work. The writers knew that they were going to have to make some traditional jabs, like making fun of the unyielding ob/gyn residents at Magee-Womens Hospital of UPMC, but Badlani, Englert, and Sobolewski had trouble finding the right songs. They scoured online databases of pop songs, trying to substitute the words with medical terms and jokes, but they couldn't find a melody that seemed to work. Every time they started to write, they recalled how funny "The Gambler" skit was. It had all the elements: a witty song, amazing choreography, and great costumes (orange camouflage and United States Marine Corps hats and T-shirts). *It's got to be like "The Gambler,"* some-

Clockwise from top: writers Sobolewski, Englert, and Badlani; producers Jonathan Bickel and Rachel Norris.

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one would say.

"I want people to look back and have them say, 'This is the funniest stuff!' and then try to outdo us next year," says Englert when asked why a medical student would become so passionate about participating in a musical.

"It's a good way to leave your mark. And it's a good opportunity to spend time with your classmates before you graduate," Englert says. "I do it for the glory; Neil is doing it for the girls—it's not working."

Aaron Bornstein, the producer and cowriter of *Saving Ryan's Privates,* in 1999, notes that every time he talks to one of his classmates about an upcoming reunion, they start by talking about their Scope and Scalpel. "It is the one thing at the end of medical school that everyone remembers and helps you to get reacquainted with your class. You leave your stamp on the school," he says.

But Englert's would-be legacy needed some inspiration. The Magee songs, or lack thereof, plagued him. Then at about 2 one morning, as he was sitting at his computer checking e-mail, he thought of "La Isla Bonita" by Madonna. It seemed the perfect solution for the ob/gyn scene. Soon, he was swapping the real lyrics for words reflecting the life of a med student working at Magee. "La Isla Bonita" became "Flagella Bonita."

And like many before them, this year's creators struggled when writing the opening act. They toyed with changing "Old Time Rock and Roll" to "Old Time Pitt Med School." Sobolewski pictured a spoof of the Tom Cruise movie *Risky Business*—a med student slides on stage, then dances around in his underwear, a short white coat, and sunglasses. The song was discarded because it was more of a solo than a number that could include the whole cast. Bornstein also recalls how much good material he and his cowriters had to throw out because there just wasn't enough room.

Even with late-night inspiration, organizing the script wasn't easy. (In December it was 72 pages long; by February, during the "cutting" process, the script had grown to 80 pages.) The

three writers had flow charts and pages of notes; they would shuffle the order, see how the scenes made sense, or if the scenes made sense. The first time the three met, they all dumped pieces of paper on the table with their ideas. (Englert wasn't the only one who kept scraps of paper with notes.) Badlani and Sobolewski had been collecting ideas since they appeared as part of their boy band, Out of Synch, in the school's 2001 talent show. The overarching theme for this year's Scope and Scalpel—which involves traveling through time—has been the same since Badlani and Sobolewski's Out of Synch performance. This year, the two, with Englert, creative director Zachary Miller, and others, made the "Braveheart" lead video for the December talent show.

"We're very attached to this show. It's our baby. It's our vision," Englert says.

"I'm concerned with the finale song," says Jessica Lin, the musical arranger. "I don't think it's a showstopper."

It is mid-January. The writers have been meeting all evening in a lecture hall in Scaife, editing each scene line by line, making the scenes punchier, funnier. Badlani, Englert, and Sobolewski are reclining in the seats in the front of the room.

"Are you talking about [the song about USMLE]?" Englert asks. "We put our strongest songs at the beginning, before the intermission, and at the end."

"It's been used every year," Lin says, referring to the tune that the writers borrowed to sing about the boards.

"The familiar is good," Englert adds.

"We always have something about the boards. It was one of the songs that stuck in our heads," he continues. This is one of Badlani's and Englert's favorite songs. Englert believes that every year there is one song that stays with everyone. Last year it was "Little Short White Coat," based on the Prince song "Little Red Corvette." The year before it was "Dahntahn," to the tune of "Downtown" by Petula Clark.

"What's a song that's a showstopper?" Bickel asks after some back and forth between Lin and the writers.

"I don't know *Rent,* but the song 'Rent' is a big singing song with a lot of voices," Lin says.

"That's what USMLE is," Badlani says.

"I wouldn't change the idea," Lin says.

"It's the '70s, and it's a '70s song," Sobolewski says.

"We had this same discussion in the script reading, and there was overwhelming acceptance," Badlani says.

"It sounds the same as the other song in this scene," Lin says.

"Everything written from '77 to '81 sounds the same," Sobolewski says. Everyone in the room giggles a little.

"We're open to suggestions," Englert says.

"This is when the musical input is important," Bickel says.

A few days later Lin expands on her comments. "What I was hoping for was something that really created tension and was exciting—not just building tension with the plot, but with the song."

"This show is unique because it takes the themes to a different level," Lin says; she wants to challenge the writers to raise their expectations of the music, too.

After the meeting, the writers and Lin talked again. The writers explained how the song might be weak from a musical standpoint, but it has strong production value because it is interactive.

Lin has been playing the violin for almost 26 years. She trained at the San Francisco Conservatory of Music. She, like the other 50th-anniversary show leaders, wants this production to stand out. Ideally, she would like to create a complete score for the production, as a movie would have.

After witnessing the discussion between Lin and the writers, Bickel notes that it's common for writers to strongly defend parts of the script during early production meetings. Lin seems to be able to sum up the writers' feelings: "There is a core group of people who have really been living this idea for a long period of time, and I think it's difficult to bring in new people."

Meanwhile, coproducer and future emergency room physician Norris has been trying to raise enough money to heighten the professionalism of Scope and Scalpel. Make it a real theater event. (And why shouldn't she dream? As alum Bornstein notes, Scope and Scalpel is the biggest medical school production. His colleagues at Children's Memorial Hospital in Chicago can't believe that each class raises at least $20,000.) Norris knows something about stage presence. After attending UCLA, she and a friend would write songs that Norris performed in coffee shops. But now, her cabaret days seem far away: There are 7,000 envelopes that need to be stuffed, sorted, and sent to alumni to secure ticket reservations. And there's the issue of increasing ticket prices: Is $10 too much to ask? Norris really wants to make this an event that includes more of Pittsburgh. The leaders of Scope and Scalpel had hoped to have the 50th-anniversary show at the Byham Theater, downtown. Yet, just to secure the Byham, the group would have had to pay nearly $10,000 for stage labor—not including the additional cost for rent. In all, the Byham would have cost close to $20,000 and restricted rehearsal times. It just didn't seem feasible.

In Englert's apartment for the first full script reading, Sobolewski speeds through the lyrics to the last song. Englert and Badlani can't keep up.

Badlani and Sobolewski had been collecting ideas since they appeared as part of their boy band, Out of Synch.

Six o'clock rounding hour. Getting pimped makes us cower. Crash and burn, relearn, third year makes your stomach churn. Wear your scrubs and ID, attending knows who you be…

Some of the viewers clap. Someone suggests showing pictures of med students and favorite professors during the last number.

"I love the song. It's a fabulous ending," says Elizabeth Legnard, one of the show's directors.

"The verses need to be prerecorded," Norris says (because the song is so fast).

"Where do we go from here?" Bickel asks.

The writers will put the scenes on the Web site for the other classmates to read and help with the editing.

"Final script?" Bickel asks.

"You tell me," Englert replies.

"February 15." ■

C.E. MITCHELL

Scope and Scalpel turns 50 on May 21 and 22.

Ronna Campbell readies Sophia, left, for ballet class, while Isabella, right, helps in her own way.

HOW DO YOU DO IT?

PARENTING DURING MED SCHOOL

BY HATTIE FLETCHER

Ask Sophia Lichen what she wants to be when she grows up, and she smiles from under her short, dark bangs, showing the spaces between her baby teeth.

"A doctor and a mommy," she answers firmly.

Sophia's mom, Ronna Campbell (Class of '04), remembers the time Sophia put on a big old shirt. A painting smock, Campbell suggested. Sophia shook her head and smiled. "No," she said. "It's my doctor coat."

Campbell looks over at Sophia, sitting next to her younger sister, Isabella, and asks if she still wants to take care of grown-ups, not kids. Sophia nods her head.

Then she climbs into her mom's lap. "I want to take care of you," she giggles, tugging on the strings to Campbell's hood and touching her mom's face.

Campbell, who plans to go into emergency medicine, isn't pressuring her daughters to be doctors—after all, they're only 3 and 5—but she finds it encouraging that Sophia, who was 8 months old when Campbell started medical school, understands what her mom is working for and wants to do something similar.

On the other hand, when Campbell looks down, smoothing Sophia's hair, and asks, "Do you still want me to be a doctor?" Sophia shakes her head no. It turns out wanting to be a doctor and a mommy is different from *having* a mommy who is a doctor. Sophia, perhaps unsurprisingly, would like her mommy to be just a mommy.

"What time are you coming home today?" she asks as Campbell gets ready to leave the family's home in Highland Park every morning.

"As soon as I can," Campbell tells her. "Maybe around six."

"That's not early!" Sophia exclaims, with the unimpeachable logic of a 5-year-old. She extends a counteroffer. "How about three o'clock?"

Of course, this predicament is familiar to most working parents, though medical school, with its reputation for being grueling even without the added pressures of pregnancy and caring for small children, might seem a particularly difficult time to start a family.

Yet most medical students who are parents say that although the schedule is demanding, notably during third-year rotations, it can also be surprisingly flexible, especially early on when there are some free afternoons and a summer off. Most weeks, Campbell is able to take Sophia to her 4 p.m. ballet class, and she has made it a rule not to study at home or on weekends. And though she didn't plan to have her second child so soon after the first, she's very pleased with the way things have worked out. She expects her residency—at the Mayo Clinic—will be more challenging for her family than medical school has been. (Campbell's husband, Peter Lichen, a researcher, hopes to take a leave away from work during his wife's residency.)

Actually, medical school can be a great time to start a family. This is especially true at Pitt, which prides itself on attracting "nontraditional" students (loosely defined as anyone over 25). It's hard to know how many of these are parents, but the numbers appear to be on the rise. The administration is committed to helping every student succeed, and though most parents try not to ask for special treatment, they say they are reassured to know that support is available if they really need it. It's not uncommon for new mothers (and even a few fathers) to take time off, even if they had not planned on doing so.

While pregnant with Isabella, Campbell told an adviser, Kathleen Ryan, that she would take a month off to have the baby. Ryan, associate director of the Office of Medical Education and an associate professor of cell biology and physiology, asked, "Why only one month?" She suggested spreading a year of course work over two years, allowing Campbell more time with her baby. Ryan talked to other administrators and smoothed the process. Campbell now says that the year of Isabella's birth was one of the best parts of her medical school experience.

"That made a huge difference," she says. "It allowed me to feel very satisfied with the time I had with my children and the time I had for school without compromising on either one."

And though being a parent may slow down the process of becoming a doctor, it can also complement it. Peter Harewood (Class of '06) studied development during his wife's recent pregnancy and says he has retained those particular lessons better than some others. (There's a flip side, though: He also remembers sitting in class and cringing as he learned about new diseases, thinking with each one, "Could that happen to the baby?")

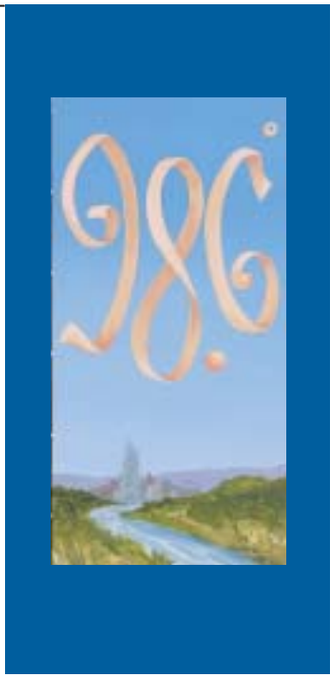
Parenthood may also make some students more compassionate doctors. Campbell remembers being a little surprised by the extent to which some of her colleagues, while loving the kids they worked with during the pediatrics rotation, saw the parents as unnecessarily anxious and difficult. You're likely to be more sympathetic, she says, when you know firsthand what it feels like to be at the doctor's office with a sick child. Some of her classmates say they also feel being able to draw on their experience as parents has enhanced class discussions and rotations, perhaps benefiting students who haven't had that experience yet.

Ultimately, what most parents enjoy about starting a family during medical school is that despite occasional moments of craziness, it provides an antidote to the potentially overwhelming pressure to study all the time. Ronna Campbell is a typically intense, competitive medical student, but having a family makes her come home and forget about work. She feels that having children has actually made her a better, happier medical student.

"People say to me, 'I don't know how you do medical school with kids,'" she reports, "and I say, 'I don't know how you do it *without* a family.' It seems like it would just consume you, and with a family that doesn't happen." ■

C.E. MITCHELL

People and programs that keep the school healthy and vibrant



CATCH THIS

BY CHUCK STARESINIC

Warning: There appears to be an outbreak of the entrepreneurial bug among University of Pittsburgh scientists. Those who are infected may find themselves in unfamiliar territory.

For example, researchers who have spent the past decade or three happily preoccupied with, say, the human immune system or neurotransmitters may find themselves unexpectedly curious about patent law and the elements of a business plan. Anyone wondering what the difference is between getting $1 million from the National Institutes of Health and getting $1 million from venture capitalists has likely contracted the entrepreneurial bug.

Local experts say that the Pittsburgh Life Sciences Greenhouse (a metaphorical, not literal, greenhouse) is both partly responsible for the outbreak and quite helpful with providing relief from symptoms. Both University research and private enterprise seem to be thriving in the Greenhouse environment.

Ruth Modzelewski, an instructor in the Department of Medicine, Division of Hematology-Oncology, apparently caught the bug on a laboratory "fishing expedition" in 1999. She and two colleagues tested a huge biological library of peptides against two different types of endothelial cells, the cells that line blood vessels. One cell line was derived from the blood vessels of tumors and the other from normal endothelial cells. They found a single peptide that was exactly what they were looking for: It seemed to bind to endothelial cells in the blood vessels of tumors while ignoring those in normal blood vessels.

They started on a poster presentation for the Society of Surgical Oncology, knowing that anything that zeroed in on a tumor had a slew of potential applications. It was as if they'd discovered a courier service that delivered to only one address, the tumor. Just thinking about the things that doctors would love to entrust to such a courier—chemotherapy and imaging compounds, for starters—was exciting. Then the society suddenly bumped them up from a poster to a platform presentation. That's when someone ventured, "Maybe we ought to patent this."

Not all scientists are interested in seeing their discoveries all the way to commercial application, Modzelewski acknowledges, but she'd been thinking about it from the beginning.

"Before we even had our results, we saw the pathway to application," she says. "That's the entrepreneurial thing. It was our baby before we even had the peptide in hand. It was our dream to have this application and see it through the whole way."

Modzelewski

Pitt's Office of Technology Management and Limbach Entrepreneurial Center (now the Office of Enterprise Development) helped Modzelewski navigate the business side of things, like writing a business plan for a new company, finding a potential CEO, and the basics of licensing a University patent. Then, in 2002, the Greenhouse was created, and that meant dramatically improved prospects for Modzelewski's efforts and the entire biotech enterprise of Southwestern Pennsylvania.

The Pittsburgh Life Sciences Greenhouse (PLSG) was launched in the spring of 2002 with $33 million from Pennsylvania's share of settlement money from lawsuits against tobacco companies. Pitt and Carnegie Mellon University were already working on bioscience planning collaboratively, but PLSG expanded this effort to a partnership that included both universities, the commonwealth, UPMC, and the regional foundation community.

PLSG was conceived as an economic development program designed to build on the region's existing strengths in biotech. The Greenhouse aims to draw established biotech companies to the region, spur the emergence and growth of new companies, direct resources to the research enterprise at the universities, attract venture capital investment, and generate contributions from local foundations.

What does that mean for the School of Medicine? In its two years of existence, PLSG has contributed $6 million to increasing laboratory space at the University, including $4.5 million toward the $188 million Biomedical Science Tower III, now under construction. The Greenhouse has even helped to recruit stellar faculty and their research teams. The University does the recruiting, but the Greenhouse can provide laboratory space, equipment, and even graduate student support.

Stephen Badylak was one of those faculty members attracted in part by the Greenhouse. Before being recruited to Pitt's McGowan Institute for Regenerative Medicine, Badylak was at Purdue, where he had been working since the late 1980s to develop "bioscaffolds" for soft-tissue and organ repair. The scaffolds are made of an extracellular matrix derived from pig tissues, and they are used to treat a wide range of defects, ranging from torn rotator cuffs to postmenopausal urinary incontinence. The body recognizes the scaffold as a template for rebuilding whatever type of tissue is required—whether tendons or urinary sphincters. Within a few months, the tissue rebuilds itself, and the bioscaffold is totally absorbed by the body, leaving little sign that it was ever

there. Marketed by DePuy, a Johnson & Johnson company, the material has been used in more than a quarter million patients in the past three years.

At McGowan, Badylak is continuing to investigate new uses for these tissues, including repair of heart muscle. In Pittsburgh's new Greenhouse, he sees a proactive organization that knows how to put industry and academia together, and experience tells him that is the way to get novel products and procedures to people who need them.

C.E. MITCHELL

The Pittsburgh Life Sciences Greenhouse seeds biomedical technology in the region with offerings like its new business incubator space in the Cellomics building on the Monongahela River.

"There are an awful lot of universities that say they have start-ups and incubators, but very few of them work well," says Badylak. "This one works."

"There is no shortage of regional initiatives in biotechnology," notes Don Smith, university director of economic development for both Pitt and Carnegie Mellon and the former interim CEO of PLSG. "At last count, there were somewhere in the neighborhood of 26 regions that we know of that were pursuing life science strategies." What makes PLSG unique, in addition to the combined strengths of two top-tier universities, says Smith, is that "most of the other regions are pursuing academic strategies or commercial strategies. The power of our initiative is that it brings the university community, the business community, the foundation community, and government together."

Doros Platika, the Romanian-born CEO of PLSG, looks outside the United States to put PLSG in perspective: "The only ones that have this kind of scope, and actually much greater scope, are outside the country. Singapore has committed $3 billion, and they have a superb university there which collaborates with the British universities, Cambridge and Oxford. There's another in Glasgow. Also, Kobe [Japan] has committed over $1 billion." But in the United States, Platika says, the scope of an organization like PLSG is fairly unusual. More than $100 million has been committed to PLSG by the commonwealth and private foundations.

Ruth Modzelewski received a lot of support from PLSG as she formulated her business plan. Last November, PLSG awarded her funding through its Technology Development Fund, which supports research into early stage inventions to increase the likelihood that the technology will be successfully commercialized through a regional start-up.

Now Modzelewski has her hopes set on the PLSG Incubator, a fully furnished and wired laboratory/office space on the Monongahela River. The incubator is designed to support life science companies in their early stages and to provide temporary space for companies relocating to the Pittsburgh area.

Modzelewski admits that the entrepreneurial bug can lead to fatigue—it's like asking for a second job—but it also seems to confer optimism. She sees multiple benefits to the creation of Trism. (Her company name was inspired by the three amino acids in her peptide as well as the city where it was discovered.) "I'm a native Pittsburgher," she says, "so it would be really cool if we could contribute something to the economy of the area through establishing a company, along with doing what we ultimately hoped to do, which is to improve cancer therapy." ■

BOOSTER SHOTS

At the recent Heinz Hall gala to benefit the University of Pittsburgh Cancer Institute, 46 major donors were presented with medallions. Together, they make up the **Circle of Hope**, a group of supporters who each contributed $10,000 or more to cancer research. Far from strangers, more than a few of them might regularly pass each other in the halls of the Hillman Cancer Center. In addition to former patients and community supporters, the Circle of Hope includes eight UPCI physicians and scientists. Among them, Professor of Medicine **Ronald Herberman**, the director of UPCI and UPMC Cancer Centers and Pitt associate vice chancellor for cancer research.

Ever wonder where your donation to the Medical Alumni Association went? Rest assured, one outstanding Pitt medical student will be glad you gave. The MAA will award a full merit-based scholarship to a student entering in 2004. (The most recent **MAA scholarship** winners, **Soyoung Im McFarland** and **Matthew Porembka**, are now in their third year.) If you have any doubts about the importance of such scholarships, just ask the MAA's emeritus executive director, **Ross Musgrave** (MD '43), who says, "I went to medical school on a scholarship. Without it, I would have been a steelworker." —*SKP & CS*

FOR MORE INFORMATION: 1-877-MED-ALUM
Or mhsf@ia.pitt.edu

CLASS NOTES

'30s

In 1960, **Paul Caplan** (MD '36) was shocked when he heard from the National Institutes of Health regarding the grant application he'd submitted. As a rheumatology consultant for the United Mine Workers of America, he was hoping to research the effects of osteoarthritis of the spine on the work capabilities of coal miners. The news from NIH: They didn't want to give him the $5,000 he'd requested. Instead, they thought they'd give him $25,000. Caplan, now a clinical assistant professor of medicine at Pitt and senior partner with Arthritis & Internal Medicine Associates–UPMC, has been practicing medicine since 1939. For 20 years, he traveled with the Pittsburgh Symphony as their physician on their overseas tours. Last year, the American College of Rheumatology named him a Master of Rheumatology—an honor bestowed on only 14 rheumatologists in the world. Caplan and his wife, Gertrude Caplan, recently initiated the Paul S. Caplan award to support a fellow at Pitt's Arthritis Institute.

'70s

Malcolm Orr (Anesthesiology Resident '71–'73) remembers a night in the emergency room in 1971 when he treated an 18-year-old pregnant woman who had been hit by a vehicle. Although the physicians were unable to save the baby, Orr, a former assistant professor of anesthesiology at Pitt and professor at the University of Texas Health Science Center at San Antonio, worked diligently to save the young woman, spending the entire night giving her every unit of compatible blood he could find. She didn't make it, and Orr began to think about the complications associated with transfusions. He later began to research ways of harvesting a patient's red blood cells (RBCs) and developed what is called an intra-operative blood salvage system. In the operating room, the device takes blood being lost during surgery and feeds it into a centrifuge, which separates pure RBCs from other components of plasma. The RBCs are then washed with saline and given back to the patient. The recycling technique reduces the patient's need for blood products from donors, which are potentially harmful.

A. Leland Albright (Neurosurgery Resident '74–'78) is chief of pediatric neurosurgery at Children's Hospital of Pittsburgh. Early in his career, Albright became involved in developing a multidisciplinary clinic for children with cerebral palsy. To help these patients who suffer from brain damage that results in muscular impairment, the clinic offers physical therapy, occupational therapy, social work, and orthopaedic surgery. Albright's most challenging cases are children with dystonia, an abnormal muscle tightness that causes involuntary contortions in cerebral palsy patients. It's difficult to treat because the condition worsens over the course of several years and creates painful twisting of certain muscles. Albright has found that infusing the muscle relaxer Baclofen into the spinal fluid improves dystonia in 85 to 90 percent of children with dystonic cerebral palsy.

Stephen Aronoff (MD '76) started his career researching pediatric genetic diseases, specifically cystic fibrosis. When Aronoff became director of the Mountain State Cystic Fibrosis Center in Morgantown, W. Va., it was a humbling experience. For the first time, he not only conducted research, but also treated patients with cystic fibrosis, who struggled to breathe as their lungs filled with thick mucus. He remembers times when he sat with dying children, with little to offer their families except his physical presence. Aronoff spent 10 years as the director of the center and today is the chair of the Department of Pediatrics at Temple University School of Medicine. He is currently chairing a committee that is rewriting the curriculum at Temple University to be more evidence based.

Thomas McGarrity (Internal Medicine Intern '79–'80), a professor of gastroenterology at the Penn State Milton S. Hershey Medical Center, is interested in the genetics of colon cancer. His research has led him to investigate a disease known as Peutz-Jeghers syndrome, which is characterized by polyps in the small intestine and colon. After treating several patients with PJS, he noticed a cluster of such cases in families in central Pennsylvania. McGarrity has since noted that polyp tissue of these people overexpress certain proteins involved in cell growth. The discovery could lead to possible therapies.

WE KNEW YOU WHEN

WHITE COATS AND SHOULDER PADS

In 1963, the University of Pittsburgh fielded one of its greatest football teams ever, both on and off the field. More than half of the players would go on to advanced degrees. They also were ranked number three in the nation. They might have played for the title of national champions, but they failed to even appear in a bowl game that year.

It was a different era in college football, says Jock Beachler (MD '70), when almost everyone played both offense and defense. He was an outside linebacker and offensive lineman. "I was small and smart and I knew how to hold well," he says with a hearty laugh, referring to getting away with penalties. He was class president for his last two years of medical school. Today, he's an orthopaedic surgeon in Pittsburgh's South Hills.

As a 240-pound lineman, John Zabkar (MD '68) was big. Nowadays, there are quarterbacks who weigh 240. For him, the Syracuse game was a high point. Losing by 21 points at halftime, Pitt shut out Syracuse in the second half, winning 35–21 in a thunderstorm that turned to snow by game's end. Zabkar now enjoys running his Grove City pathology lab as a one-man show.

James Hogan (MD '69), the team manager, says that in their only loss, the navy team

'80s

Martin Tobin (Critical Care Fellow '82–'83), director of the Division of Pulmonary and Critical Care Medicine at the Loyola University Chicago Stritch School of Medicine, is editor of the *American Journal of Respiratory and Critical Care Medicine*. Tobin, himself, is studying the appropriate methods of weaning patients off ventilators. Half of the patients in intensive care units are on ventilators, and although 40 percent of these patients are capable of coming off ventilators, certain tests must be performed first. To determine who is ready to breathe independently, Tobin came up with an index number that is the ratio of respiratory frequency (the number of breaths per minute) over the tidal volume (the volume of air entering and leaving the lungs in a single breath). He has found the best method for weaning patients is through spontaneous breathing trials, where patients are taken off the ventilator and breathe on their own through a small tube known as a circuit.

When an investigation pointed toward green onions as a source of last year's hepatitis A outbreak in Beaver County, Pa., **Virginia Dato** (MD '83) wondered how properly cleaned onions could be the cause of an outbreak of such magnitude. One day, she and her husband, Michael Chancellor, a Pitt professor of urology, bought some green onions at a local grocery store, but instead of using them to make dinner, they viewed and photographed them under a dissecting microscope. Even after careful cleaning, they found areas inside the bulbs where dirt was present and virus could hide. Dato is an adjunct associate professor of public health practice at Pitt's Graduate School of Public Health and a public health physician for the Pennsylvania Health Department's Division of Infectious Disease Epidemiology. She worked with other health professionals on the many tasks required to control the outbreak and prevent future outbreaks, including case investigations, public and press education, high-risk situation management, and coordinating state activities with the Centers for Disease Control and Prevention.

Kevin Judy (MD '84) has been investigating photodynamic therapy at the University of Pennsylvania as a way to treat brain tumors. Though this treatment has been used for many years, Judy is studying new dyes developed by a pharmaceutical company that will bind to tumor cells and, when exposed to light, create toxins that kill the cancer cells and spare the neighboring healthy cells. The dyes typically used in photodynamic therapy are ultrasensitive to light and stay in a person for at least a month, making it difficult and sometimes painful for the patient to go outside without being completely covered. He has already tested the improved dyes in animals and plans to perform human trials in brain tumor patients. Judy, who is a neurosurgeon, first came to Penn to start a brain tumor program that combined neurosurgery, neurology, and radiation-oncology. Twelve years later, the center is one of 20 in the country funded by the National Cancer Institute.

'90s

Bradley Stein (MD '90, Pediatrics and Child Psychiatry Intern '91, Psychiatry Resident '92—'95) is an assistant professor of child psychiatry at the University of Southern California in Los Angeles and the associate director of mental and behavioral health at the RAND Center for Domestic and International Health Security. Stein recently collaborated with the Los Angeles Unified School District to develop and evaluate Cognitive-Behavioral Intervention for Trauma in Schools, a program that helps students who suffer from emotional and behavioral problems caused by exposure to multiple acts of violence, such as witnessing serious physical fights or being attacked with a knife or gun. After participating in the program, the students had significantly fewer symptoms of violence-related distress and depression than students on a wait list. Stein's interest in the study of children dates back to his days as a resident at Pitt. Early in his career, he had the opportunity to travel to Romania with a team of residents and nurses to assess orphanages. Seeing the children in the orphanages stimulated Stein's interest in the psychiatric effects of trauma on children. Later, he worked in Bosnia with children exposed to war and trauma as a consultant for the International Rescue Committee.

The Hippocratean, 1991

As an assistant professor in the department of surgery at the University of Utah, **Brandon Bentz** (MD '93) divides his time between clinical care of head and neck patients, clinical research, and basic science research into nitric oxide. He recently applied, with the guidance of his mentor John Hibbs (MD '62, see page 17), for a National Institutes of Health grant to study how nitric oxide alters tumor cell migration, which can impact how these cells metastasize. Bentz's mother, Francesca Peretti (formerly Frances Geigle-Bentz) was an associate dean in Pitt's School of Health and Rehabilitation Sciences and a colleague of Pitt Professor Eugene Myers. Myers sparked Bentz's interest in otolaryngology (as did an abscessed septum Bentz had, which prompted his visit to the ear, nose, and throat clinic). Bentz's interest in nitric oxide started when he took two years between undergraduate and medical school to work as a technician in Timothy Billiar's lab; Billiar is now the chair of Pitt's Department of Surgery.

Todd Oravitz (MD '94, Anesthesiology Resident '95–'98) wasn't sure which specialty to choose until a third-year rotation in anesthesiology, when he met Jackie Morillo-Delerme, an assistant professor. She would talk about how to insert breathing tubes and then watch as he did it, asking him questions all the while. Morillo-Delerme was always available to talk with Oravitz. In many ways, he has emulated her pedagogical style in his position as an assistant professor in the Department of Anesthesiology at the University of Pittsburgh. This year, Oravitz won the Dr. Leroy Harris Award for Excellence in Teaching, an award the residents annually bestow on the best professor in the anesthesiology department.

William Field (Surgical Pathology Fellow '96–'97) once served as the deputy medical examiner for the city of Ithaca, N.Y. Today, as president of Pathology Associates of Ithaca, his love of detective work infuses his lab work, and he discusses pathological tests as if they are cloak and dagger. Field recalls in particular how difficult it was conducting investigations into infant deaths—determining if it was murder or sudden infant death syndrome. His training at the Elisabeth Kubler-Ross Center, which teaches people how to counsel others with grief, helps him serve as a counselor with suicide prevention and crisis services.

—CB, MH, & SKP

ambushed Pitt with trick plays and a solid performance by Roger Staubach. After decades in a downtown Denver ER, Hogan is enjoying the slower pace of Boulder. Every once in a while, he takes a long look at the faces in his 1963 team photo.

John Verkleeren (MD '71) can recall the thrill of making a tackle and catching a pass for a first down in his first game, against UCLA in the Los Angeles Memorial Coliseum. He spent 20 years in the navy, somehow found it in him to root for their team, and is now chief of cardiology at Kaiser Permanente in San Diego.

The season and the nation were sent reeling by the assassination of President Kennedy in November of that year. Pitt postponed its final game against Penn State; many other teams played as scheduled. The four major bowls invited teams to play before Pitt could complete its season, and the now legendary team of 1963 was left out in the cold. *—CS*

The 1963 Panthers fielded a great team that would spawn four Pitt med grads. (From left) Jock Beachler, John Verkleeren, and James Hogan are highlighted below. John Zabkar is not shown.

THE WAY WE ARE

MINORITY REUNION

There is a sense of group identity in every graduating class. Among minority students, says Paula Davis, assistant dean of student affairs in the School of Medicine, there exists a slightly different sense of family, which links students across graduating classes. To strengthen and celebrate the family, the first-ever minority reunion was held April 16–18 in Pittsburgh. A few family portraits:

In the small town of Webuye, Kenya, **Clarissa Dudley** (MD '95) remembers the night when a child came into the hospital with a torn lower lip and blood dripping from his nose and wounds on his limbs. He'd apparently fallen from a 30-foot tree. After sewing his lip (all the way to his chin), Dudley faced the sobering reality that the nearest CT scan was eight hours away in Nairobi. She asked the nurses to periodically check the boy's mental state, and advised the parents to take him there in the morning. It was baptism by fire for the young doctor. There were times Dudley felt that she had learned more from the Kenyans than she was able to provide them in return. They taught her about the role that culture and belief systems play in healing, that dependence on technology can diminish both diagnostic skills and the doctor-patient relationship. Her time in Kenya ignited her interest in international health. Since completing a master's degree in public health at Johns Hopkins University, Dudley has worked as a *locum tenens*—a physician temporarily assigned where medical services are lacking—in Vietnam and the Philippines.

Dudley

At some time in the early 1990s, **Levi Downs** (MD '94) stood in front of his classmates in the School of Medicine and gave a presentation on protecting a patient's airway and clearing it of obstructions. Right about then, Downs suspected how fulfilling it would be to teach medicine and hasn't looked back since. Downs, currently an assistant professor in the Department of Obstetrics, Gynecology, and Women's Health at the University of Minnesota, got a big boost from Pitt's Prematriculation Program, which gave incoming nontraditional and minority students a sneak preview of the courses they take in their first year of medical school. Downs now teaches medical students in problem-based learning sessions and trains residents in gynecology.

Downs

When he was a first-year medical student, someone told **Michael Forbes** (MD '90), "Racism is like rain. When it's raining, you pull out your umbrella. But when it's not, you enjoy the sunshine." Forbes, now an assistant professor of pediatrics in the Drexel University College of Medicine, is happy to report that he has felt more sunshine than rain as a practicing physician. His specialty is pediatric critical medicine, and he finds his most challenging cases are infants with bacterial infections. He is currently writing a book, *No Satisfaction: When Mental Illness Comes to Church*, which addresses mental health issues such as mood disorders, neuroses, and schizophrenia within the church community and urges the medical community to incorporate spirituality into the practice of medicine. Forbes is an ordained minister.

–Sonya Kanti Patel

Forbes

IN MEMORIAM

'50s

JOSEPH C. MULL (MD '51)
JULY 20, 2003

DAVID L. MCANINCH (MD '53)
FEBRUARY 29, 2004

CLAYTON E. CULBERTSON (MD '59)
DECEMBER 23, 2003

CRAIG B. MILLER (MD '59)
DECEMBER 23, 2003

'60s

LAWRENCE A. DUNEGAN (MD '63)
JANUARY 9, 2004

ROBERT W. HILBERG (MD '67)
DECEMBER 24, 2003

'90s

WAYNE G. CESSNA (MD '97)
DECEMBER 26, 2003

UGOCHI OYOYO-ERONDU (MD '97)
DECEMBER 25, 2003

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HAITIAN SCREENINGS: ROSEMARY EDWARDS

BY MEGHAN HOLOHAN

COURTESY EDWARDS

Voltaire (left) draws blood from Edwards as a nurse looks on.

The drive to Fondwa in Western Haiti from Port-au-Prince takes two hours, yet the village seems centuries away from the turmoil in the capital. Most of the journey is on paved roads, but a four-wheel-drive is needed to navigate the last few miles up and down a single rutted road leading to the village. The whole area is angled hills and sloping valleys. Fondwa sits near the base of a steep mountain.

In the center of town, a three-story cement building is set in tropical foliage flanked by the primary school complex and orphanage. Not long ago, Rosemary Edwards (MD '84) sat inside that building with a tourniquet on her arm, her veins bulging blue. Nurses, nursing students, and women training to be other healthcare workers surrounded her. Sister Carmelle Voltaire, who ran the clinic, had done this before so she went first. None of the others surrounding Edwards had ever drawn blood—in Haiti there is very little hands-on teaching. Some of the students had never seen a needle like the one they were about to use.

Edwards, a pathologist at Mercy Hospital in Pittsburgh, wanted them to learn on her arm because her veins are easy to see.

Voltaire felt Edwards' arm for a vein, then slid the needle into it; immediately, blood flowed into the collection tube. After she cleaned her equipment and disposed of the needle properly, a young student set out the instruments she would need to draw blood for her first time.

A week later, Edwards' arms are still black and blue from the half-dozen times the students practiced on her arm. But she's pleased, because all of the students successfully drew blood with the same ease as Voltaire.

As a medical student, Edwards always thought she would be a doctor in a developing nation. But as she started her career, she also started a family. So she pursued her practice and put other aspirations on hold.

She first went to Haiti in June 2001 as part of Global Health Ministry (a program of Catholic Health East). Before departing for Port-au-Prince, a friend referred her to Rich Gosser, a professor at St. Vincent College, in Latrobe, Pa. Gosser, executive director of Partners in Progress, has been taking U.S. citizens to Haiti to collaborate with rural communities since 1999. A few years ago, he was in the basement of the Sacred Heart Church in Shadyside, packing medical supplies for an upcoming delivery to Haiti, when Edwards asked him questions about what it was like there. He gave her rushed answers, not really expecting that he would hear from her again. Many times people go on one volunteer trip, he says, and they never do it again.

"Everyone always talks about doing something like this—*Someday I'm going to travel or write,*" says her son Chris Edwards. "I was really proud of her when she actually did it."

Back in Pittsburgh, Edwards took classes in sustainable development, micro-credit financing, and environmental sciences. If she was going to be of lasting help, she was going to need to be innovative, like many of the Haitians she'd met.

There were plenty of issues to tackle. Anemia can be a big problem for women in developing nations, Edwards notes. In the United States, women can afford iron supplements or eat meat to make up the deficiency. In Haiti, most people cannot afford these things. So Edwards and the Fondwa staff discussed inexpensive iron-rich foods that Haitians could easily obtain, such as leafy-green vegetables, beans, and lentils.

While Edwards was learning more about Haiti, Partners in Progress was working with the Association of Peasants of Fondwa, the organization that founded the local clinic that serves 42,000 people. The two groups were hoping to build a pathology lab, and Gosser recruited Edwards, the doctor with a basement full of questions, to help. She agreed to visit the village to see if it was feasible. ("She was never one to jump before she knew where she would land," says Chris Edwards.) The project appeared feasible, with a little improvisation. The first obstacle: The electrical grid didn't extend into the countryside. So Edwards secured funding for a photovoltaic solar power system. With Partners in Progress, she also won a grant to pay for laboratory equipment and supplies.

But translating finer points of providing care can be more difficult than finding electricity in rural Haiti, Edwards has found.

In Haiti, not everyone embraces American medical ideals, like respect for patient privacy. Edwards' Haitian colleagues were concerned such issues hampered their ability to provide care. Many Fondwans won't get tested for HIV or tuberculosis because afterward, the whole village ends up learning the results. So Edwards has tried to lead by example, pulling each patient aside into a private room. Yet some villagers are still curious. They'll even ask her about the test results of others. When that happens, Edwards just says: "I'm sorry, I am not privileged to tell you that information." ■

Titles suggested by students for this year's Scope and Scalpel:

HARRY CLOTTER AND THE CHAMBER OF SECRETIONS
ALONG CAME A POLYP DUDE, WHERE'S MY RETINA?
LOST IN TRANSPLANTATION FINDING CHEMO
MASTER AND COMMANDER: THE FAR SIDE OF THE WARD
FATAL IMPACTION *WIZARD OF GAUZE*
20,000 COLLEAGUES UNDER MAGEE SQUIRMINATOR 2: MATCH DAY
MYSTIC LIVER THE MATRIX: REIMPACTED
NO SEX IN THIS CITY XXY BORED OF ATTENDINGS
A LONG DAMN FOLEY SPIDER ANGIOMA MAN
GLOVE ACTUALLY 50 FIRST RECTALS
FERRIS BULLAE'S DAY OFF *DIRTY DRESSING, PRESBY NIGHTS*
MEDICAL SCHOOL, INTOLERABLE CRUELTY
HERPES ARE FOREVER LORD OF THE INGUINAL RING
SOMEONE'S GOTTA LIVE *FRIABLE GREEN STOMAS* *1460 DAYS LATER*
DON'T KILL BILL: VOL. 1 *PETER PANUS* GOUTY
MEET THE RESIDENTS *WEEKEND AT MOSER'S* BRIDGET JONES' DIARRHEA
DIAMOX IS FOREVER *SCHOOL OF DOC*
BILL & TED'S EXCREMENT ADVENTURE *AROUND THE WARD FOR 80 DAYS*
WHOSE SPINE IS IT, ANYWAY? AN ORIFICE AND A GENTLE HAND
MED STUDENTS: CHEAPER BY THE DOZEN EVERYBODY LOVES PHLEGMON
FINDING PNEUMO *CAN'T HARDLY INTUBATE*
COLD HANDS LUKE THE MAN WITH ONE RED, RUBBER CATHETER
DIAL D FOR DISIMPACTION DR. EIBLING, THE LAST SAMURAI
C. DIFF SKIT STAR WARDS EPISODE 50: ATTACK OF THE LOANS
OLD STOOL HOW TO LOSE AN EYE IN 10 DAYS *BIG FISTULA*
THE WIZARD OF OSTOMY BABINSKI AND CROTCH

and the winner is **LASIX UNLOADED**

CALENDAR

OF SPECIAL INTEREST TO ALUMNI AND FRIENDS

MEDICAL ALUMNI WEEKEND 2004
MAY 21–24
Classes celebrating:

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

SENIOR CLASS LUNCHEON
MAY 21
11:30 a.m.
Twentieth Century Club
Pittsburgh

SCHOOL OF MEDICINE SCHOLARSHIP TEA
MAY 21
3 p.m.
Pittsburgh Athletic Association

SCOPE AND SCALPEL *LASIX UNLOADED*
MAY 21 & 22
The Antonian Theatre, Carlow College
Pittsburgh
7 p.m.
For information:
www.pittmed.pitt.edu/sas/2004

DEAN'S BREAKFAST AND ALUMNI DINNER
MAY 22
8:30 a.m. and 6 p.m.
Sheraton Station Square
Pittsburgh

ESTATE PLANNING BREAKFAST
MAY 23
9 a.m.
"Take a Bite out of Estate Taxes"
Sheraton Station Square
Pittsburgh

GRADUATION CEREMONY
MAY 24
10 a.m.
Carnegie Music Hall
Pittsburgh
For information:
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412-648-9040
student_affairs@medschool.pitt.edu

CLASS OF 2008 WHITE COAT CEREMONY
AUGUST 15
Scaife Hall, Lecture Rooms 5 & 6
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C. 1902, TWINS HENRY AND EDNA JULSETH, THE LATE GRANDFATHER AND GREAT AUNT OF ERICA LLOYD, OUR EDITOR IN CHIEF

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