UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | JANUARY 2002

# PITTMED



## SOMETHING LIGHT

SCOPE AND SCALPEL KEEPS TICKLING OUR FANCIES




## A GOOD APPLE

Dr. Levine's comments in the July issue brought back a flood of memories for me. For I, too, had the privilege of studying under Dr. Franklin Reeve while at Columbia. Dr. Reeve was my preceptor for literature humanities during the first semester of my sophomore year.

For a naive 17-year-old product of academic acceleration in the New York City school system it was a revelation. More than anyone else he opened my eyes to the richness of literature and philosophy, an appreciation that I've maintained on some level to this day. His Russian influence must have been there as well for I took a Russian literature course as an elective in my senior year, which I also cherish. It's been a long time since I thought about Professor Reeve. Thank you, Dr. Levine, for writing your article, which allowed me to relive some of those pleasant emotions.

Ralph Schmeltz, MD '63
Clinical Professor of Medicine
University of Pittsburgh

## WE YEARN FOR JERNE

The October article on Niels Jerne captures much of the personal charm as well as the innovative scientific insight that characterized my blood cousin. I've sent a copy to his wife.

*Pitt Med* is a real winner among the alumni journals published in the United States. The October issue was especially attractive from Chancellor Nordenberg's call to the campus community on September 12 to Dr. Einstein's photo from 1934.

Campbell Moses, MD '41
New York, New York

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

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***Pitt Med* Honors, 2001**

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**You—yes, you—can help your beloved alma mater ensure it keeps graduating the best and the brightest students. The Office of Admissions at the School of Medicine is looking for alumni to touch base with admitted applicants from all over the country. Maybe you could meet with Pitt prospects over coffee, answer their questions by phone or e-mail, or invite them to your clinic or lab. (If you're a recent grad, don't think that applicants wouldn't enjoy hearing your point of view as well. You are perhaps best equipped to let them in on what they can expect after they enroll.) What better way to tout our school than to show off Pitt's finest?**

**To find out more, call 412-648-9891.**

# PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE | JANUARY 2002, VOL. 4, ISSUE 1



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## CONTRIBUTORS

DAVID R. ELTZ—["Trial Runs" and other stories] David Eltz didn't grow up wanting to be a writer. His first dream was football, but he soon realized he lacked talent for the game. It was only after four years in the army—where he jumped out of planes and drove armored personnel carriers—that his sights focused on writing. The soldier ended up writing for the *Pittsburgh Tribune-Review* and *Pitt Magazine*. In 2001, Eltz became senior editor of *Pitt Med* and the father of an "incredibly ambulatory" son, who is now nine months old. EDWIN KIESTER JR—["Spock's Baby"] His story on the famous Dr. Spock was written with reverence, but also a touch of envy. Spock's *Baby Book* (1946) has sold 50 million. Edwin and Sally Kiester wrote *Better Homes and Gardens' New Baby Book* (1977); it has sold 6 million. MICHAEL LOTENERO—["At The Bottom of Despair" and "No Coffee, Thanks"] This Pittsburgh artist assures us that everyone in his family draws—"everyone"—though we're not quite sure if this includes the family cat, Kalman. Nonetheless, some of Lotenero's own illustrations are scheduled to appear in a Gingko Press collection by Marshall McLuhan that was designed by David Carson. See more at http://www.lotenero.com.

## COVER

They flew the coop with a heck of a flourish. Forty-eight years of Scope and Scalpel productions have helped graduating students soar. (Photo: Don Farrall/Photodisc.)

# PITTMED

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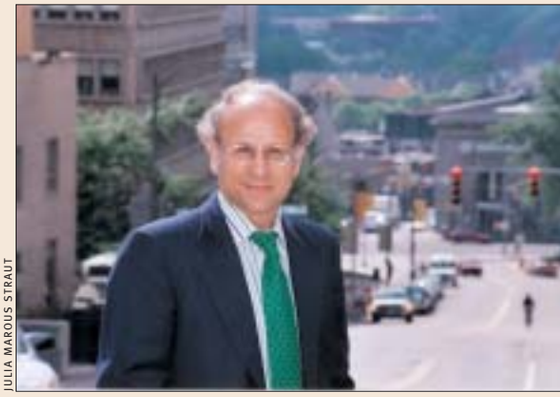
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JULIA MAROUS STRAUT

Zane Gates, a 1995 alumnus of Pitt's School of Medicine, is a recent first-time author of a medical thriller (*The Cure*) about a boy whose blood contains an element that promises a cure for cancer. Dr. Gates, who has also established a clinic aimed at the uninsured working poor, will devote a portion of the proceeds from his book to an after-school program that he set up in the Evergreen Manors housing project in Altoona. Evergreen Manors is where he grew up, and his intent with the after-school program is to expand the view and the aspirations of the children who live there beyond the apparent limits of their provenance. Dr. Gates exemplifies the physician's historic social contract just at a time when the economics of our profession make it increasingly challenging for physicians to practice in accord with this contract.

I have written frequently in this column about our school's goal of producing more scientifically astute young physicians, ones more likely to engage in clinical and basic research—given the extraordinary opportunities that are now before us consequent to the Human Genome Project. I have commented especially on how we hope to weave the excitement of discovery into our curriculum, but the fact is that we also need many more Dr. Gateses—ideally, we seek to foster the scientist and the humanist in the same person. Indeed, in the medical education literature of the day, there is a growing emphasis on humanistic factors in the medical school admissions criteria and selection processes. This discussion has reached the level of formalism, with the Liaison Committee on Medical Education (LCME), the National Board of Medical Examiners (NBME), the Accreditation Council for Graduate Medical Education (ACGME), and the American Board of Medical Specialties (ABMS) all seeking to verify that young physicians demonstrate the interpersonal and communication skills that will allow them to establish doctor-patient relations of high order.

The clear implication is that medical school admissions committees must now take up the daunting challenge of moving far beyond the cognitive threshold of the MCAT and the science GPA as they increasingly probe medical school applicants for such qualitative variables as compassion, altruism, respect for others, empathy, integrity, leadership, and a deep sense of social awareness and social justice. Dr. Jordan Cohen, president of the Association of American Medical Colleges (and a member of our school's Board of Visitors), has even suggested that perhaps we should look for these qualities in our applicants first, and consider the MCAT and GPA only after the applicant pool has made the "first cut." Since new emphasis is being placed on licensure testing of the characterological attributes of our profession, it is evident that we must assay for those attributes in the admission process and, of course, nurture those variables during the four years of medical school. Already, Pitt is doing much along these lines, yet this is hardly a facile exercise, either for the applicant or for the school. Neither scientific creativity nor committed humanism reduces to a metric, yet if we are to reassert the nobility and the autonomy of our profession, we must flavor our admissions criteria with a qualitative but critical subtlety.

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 http://www.health.pitt.edu*

# Honored Twice Over by Howard Hughes

An organ waiting to be transplanted is chilled to 4 degrees Celsius. When the organ is placed in its recipient and reattached to a blood supply, the blood suddenly flowing through the cold organ damages it, inflicting cold ischemia reperfusion injury.

Last year, Gautam Yagnik, MD '03, worked in the lab of David Geller, the Samuel B. Harbison Assistant Professor of Surgery, where he explored the use of the amino acid L-arginine to reduce cold ischemia reperfusion injury and showed that it was of benefit. Yagnik's year in Geller's lab was funded by a Howard Hughes Medical Institute (HHMI) research fellowship.

This academic year, Yagnik received a second honor from HHMI—a continued support fellowship. Of the 53 medical students from around the country who received an HHMI research fellowship in 2000, only 13 were selected to receive the continued support award. The grant provides Yagnik with $34,000 per year during his last two years of medical school.

Pitt must have good HHMI karma, and good potential investigators. Genevieve Ambrose, MD '04, and Kevin Sullivan, MD '04, both received HHMI research fellowships this year. *—DH*

PATRICIA NAGLE



Yagnik

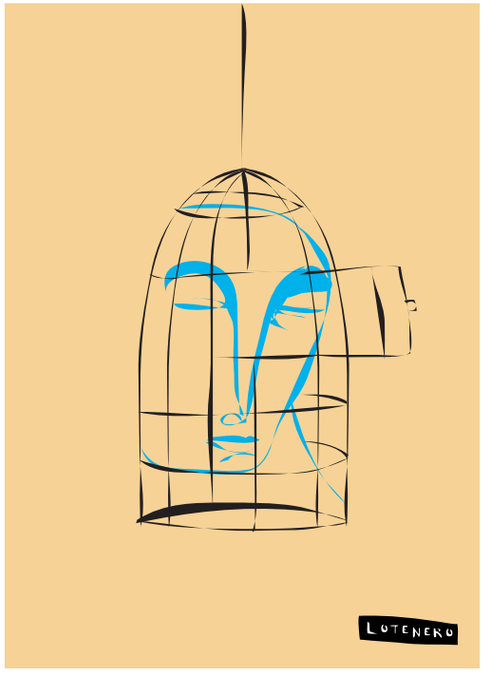
## FOOTNOTE

Dan Lesser, he's quick. We don't say that because the third-year Pitt med student garnered a Society for Pediatric Research fellowship or because he's bright. We mean he's *really* quick—whoosh, zip, vroom kind of quick. The former New York state cross-country champ beat all other Pittsburghers in the Great Race and in the Pittsburgh Marathon in 2001. The marathon, his first, took him just 2 hours, 35 minutes, and 35 seconds—with an injury.

## SMALL DOSES OF HAPPINESS

At a solo concert last May, the PalPITTations, the medical school's new a capella group, debuted some lyrics the members wrote themselves. "We sang a song poking fun at the [graduating] fourth years, who every single day would send us multiple e-mails trying to get us to buy their various garbage—futons, televisions," says group president Zachary Miller, MD '04. They might nudge a graduating class along the way, but the performers, now 24 strong, make it clear that their playful lyrics are all about spreading cheer. "Our hope is that we bring happiness on a small scale," says Miller. The PalPITTations already have brightened spirits at Children's Hospital of Pittsburgh, alumni events, the Mini-Medical School graduation, and this year's meeting of the Association of American Medical Colleges. *—DH*

TO ORDER A CD: zam1@pitt.edu




## AT THE BOTTOM OF DESPAIR | BY DOTTIE HORN

A patient with end-stage kidney failure wants to be taken off dialysis. With the treatment, she's likely to live; without it, she will die in a matter of days, perhaps weeks. It may be the inescapable burden of dialysis that has put her in this state of mind. Or it may be that she feels abandoned by her spouse or overwhelmed by disappointments. If presented with a thoughtful plan of care that takes emotional and other issues into account, this patient is likely to choose to continue treatment—and give herself a few more years. Before this can happen, her physician must know how to talk to her, to get to the bottom of the despair.

A medical student may be intimidated at the thought of having that conversation. David Barnard, professor of medicine at the University of Pittsburgh, wants medical students to know how to negotiate such difficult conversations—and to be well informed about a spectrum of end-of-life care issues. With the help of a four-year, $750,000 grant from the National Cancer Institute, Barnard will make end-of-life issues a more prominent part of the education of every Pitt medical student.

Barnard will use the grant partly to develop new material for the first- and second-year curricula. The grant will also support training workshops for clinical faculty members who teach students in the third and fourth years and a pilot program in which 12 Pitt med students regularly visit patients who are terminally ill.

"In a typical medical school, students can go through all four years of training and never actually spend time with a patient who is dying," says Barnard. "There's a mismatch between the way medical education is set up and the needs of dying patients. It's that mismatch we are trying to address."

# Faculty Snapshots


Harrison

In Maryland, the incidence of meningococcal disease (which is one type of bacterial meningitis) in adolescents and young adults aged 15 to 24 steadily increased from 1990 through 1997, then began to fall in 1998. "If you look at the trends in smoking in adolescents during the 1990s, they mirror almost exactly this trend in meningococcal disease," says **Lee Harrison**, assistant professor of medicine and epidemiology. "I strongly suspect that at least some of the changes in incidence of meningococcal disease were due to smoking changes," says Harrison. His study was published in the August 8 issue of the *Journal of the American Medical Association*. Harrison is now pursuing a multistate study to see if smoking is indeed a risk factor for the disease.

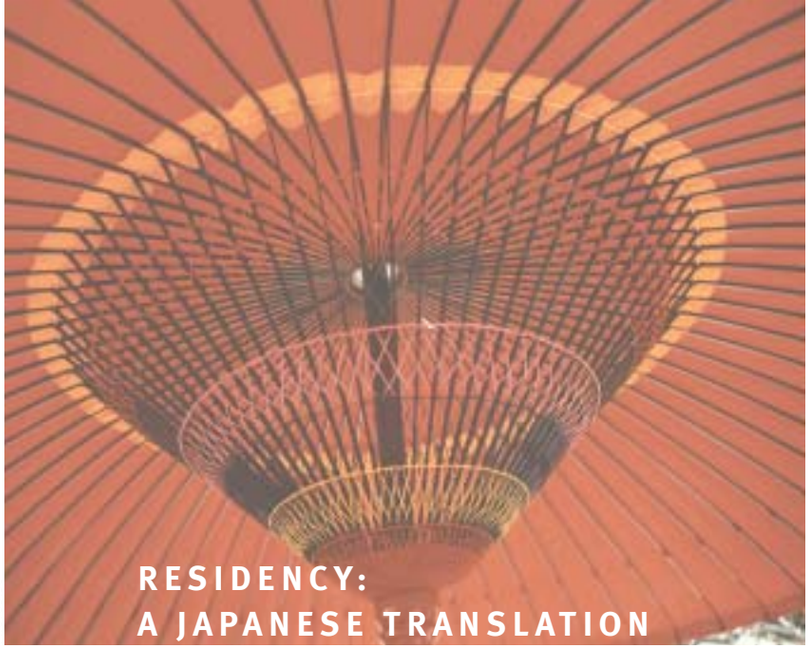
In July, the University of Pittsburgh Cancer Institute received a five-year, $12 million grant from the National Cancer Institute to study lung cancer. The award, called a Specialized Program of Research Excellence (SPORE) grant, will support five research projects. Two of the projects, led by **Jill Siegfried**, professor of pharmacology, look at why women are more susceptible to lung cancer than men. **Joel Greenberger**, professor of radiation oncology, will assess whether gene therapy can help protect normal tissue in the esophagus and lung from damage inflicted by radiation therapy. **Joel Weissfeld**, associate professor of epidemiology, will focus on the use of multidetector CT (computed tomography) to detect lung tumors when they are extremely small and likely to be curable. **Olivera Finn**, professor of immunology, will examine the protein cyclin B1 as a possible vaccine against one type of lung cancer.


Still ticking after 12 hours.

HEART AND GIRL (RIGHT): COURTESY UPMC NEWS BUREAU

A human heart kept beating, outside a body, for 12 hours—to most, this sounds spooky, great fodder for the likes of Edgar Allan Poe. To **Robert Kormos** and colleagues it sounds wonderful. In October, a Portable Organ Preservation System (POPS), engineered by TransMedics, of Woburn, Massachusetts, was tested on a human heart for the first time. The preclinical test took place at Pitt and marks the longest any such device has kept a heart beating in, what appears to be, its normal physiological state. Much more testing is needed and under way, asserts Kormos, Pitt professor of surgery as well as director of thoracic transplantation and the artificial heart program. If POPS continues to meet with success (as it has in animal studies), that could mean great things for advancing transplant surgery. The "shelf life" of a heart without blood flowing through it is about six hours. POPS designers believe the suitcase-sized unit would allow organs to be transported over longer distances and reduce complications for transplant recipients. "It's very encouraging, but very early," notes Kormos. *—DH & EL*

FOR MORE ON POPS: **http://www.upmc.edu/newsbureau/tx/pops**



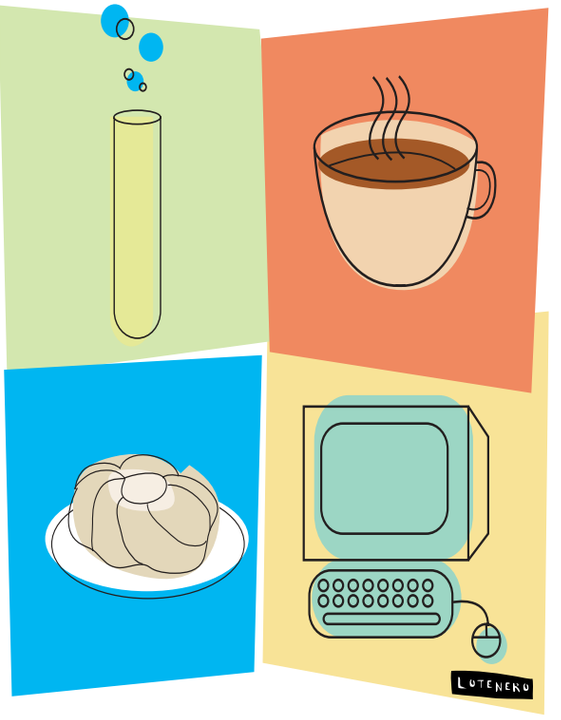
PHOTODISC

## RESIDENCY: A JAPANESE TRANSLATION

**In the United States, residency training emphasizes hands-on learning, the mastery of specific skills. As their residency continues, trainees typically take on more and more responsibility for patient care. In Japan, by contrast, residents spend little time directly caring for patients and most of their time observing a senior mentor. The Teine Keijinkai Hospital, in Sapporo, plans to establish a residency training program more like those in America—in collaboration with the School of Medicine and UPMC Health System. Codirectors of the program, which will accommodate six internal medicine residents in its first year, are Asher Tulsky, assistant professor of medicine at Pitt, and Hironori Murakami, an MD at Teine Keijinkai Hospital.** ***—DH***

# No Coffee, Thanks

An unshaven 20-something man sporting scrubs rushes into the Masonic Temple ballroom, making a beeline to the massive table covered with mountains of bagels and cheese Danish, plates of fruit and eggs, and pitchers of coffee and juice. On the other side of the room, another 20-somethinger, this clean-shaven fellow wearing a three-piece suit, is telling a TissueInformatics representative that he is perfect for the company because he will soon graduate with majors in both business and biology.



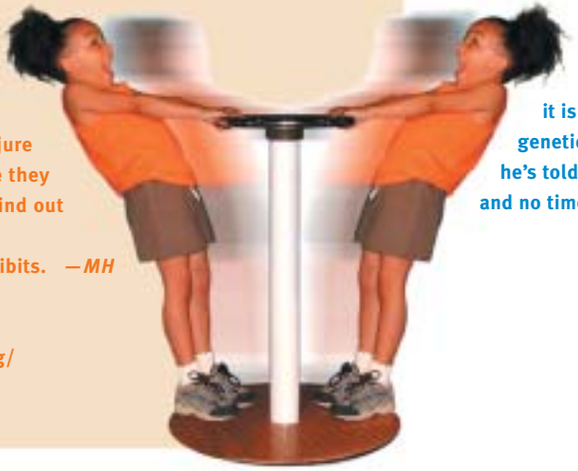

The man in the scrubs slips out after taking a few minutes to gobble the breakfast he borrowed from @PGH Café, which is one of the many events that's part of the University of Pittsburgh's inaugural three-day research festival known as Science 2001: A Research Odyssey. Most of the people here on this September morning, decidedly, do not see the food as the main attraction. The café is a relaxed-atmosphere job fair intent on recruiting science and biotech employees for 30-some Pittsburgh science and technology companies; it has attracted a total of about 300 undergraduates, graduate students, and postdocs from Pitt and other local universities.

TissueInformatics won't be scheduling an interview with the young man in the three-piece suit—not right now anyway. Today the company is hoping to fill openings for software technicians; and it is always on the lookout for cell biologists and geneticists. *Keep in touch, something might open up,* he's told. He gets out another resume—29 recruiters to go, and no time for coffee breaks. ***—MH***

# WHOA!

Head over to the North Side for a little bobsledding. You won't get cold or wet if you try the virtual sleds at UPMC SportsWorks, a new exhibition at the Carnegie Science Center. If you're eager to move beyond things virtual, there are plenty of other ways to entertain yourself there as well. Atop a 15-foot-high steel I-beam you might pedal a unicycle (that has been safely counter-weighted) or, on a 40-foot-long track, race Jackie Joyner Kersee (okay, it's only a video of the Olympic star).

Faculty members from the School of Medicine helped develop many of the educational displays that are part of the exhibits. One display, at the rock-climbing wall, shows all of the muscles used while climbing. Another discusses how women who play volleyball or basketball often injure an anterior cruciate ligament because they aren't landing properly. Visitors can find out the proper way to land.



SportsWorks has more than 40 exhibits. ***—MH***

FOR MORE INFORMATION:
http://www.carnegiesciencecenter.org/upmc-sportsworks/sportsworks.htm



It's easy to see how artist Mary Hamilton's linoleum-block images, which are infused with playfulness and animal imagery, were a welcome break at UPMC Shadyside. "It's healthy to laugh," Hamiliton notes. "And animals serve as great healers in all kinds of ways." The exhibit ran through November.

PATRICIA NAGLE

## Appointments

As the chair of Pitt's new critical care medicine (CCM) department, **Mitchell Fink**, Watson Professor of Surgery, plans to reach out to select community hospitals. Some of these institutions currently have no CCM specialists; others lack round-the-clock coverage. He would also like to see the new department further strengthen research efforts related to the epidemiology of critical illness, genetic markers for sepsis, molecular biology of traumatic brain injury, use of hypothermia to improve outcomes from hemorrhagic shock, as well as other areas. Fink's own studies focus on the effect of inflammation on organ system function in sepsis and septic shock. His research is funded by the National Institutes of Health and Defense Advanced Research Projects Agency. "We have discovered a new therapeutic agent that we think might be of value for the treatment of victims of a bioterrorist attack," he says.



Fink



Gallion

**Holly Harbage Gallion**, formerly a professor at the University of Kentucky in Lexington, joined Pitt in August. In Pittsburgh, she will direct the National Center of Excellence in Ovarian Cancer at Magee-Womens Hospital and continue her research on the early detection of ovarian cancer. By pinpointing genetic and biochemical abnormalities, she hopes to develop new methods for screening. Gallion is on the editorial board of the journal *Gynecologic Oncology* and PDQ, an online database sponsored by the National Cancer Institute.

**Olivera Finn** has been appointed acting chair of the School of Medicine's newly created Department of Immunology. Finn's goal is to attract "hungry" investigators who want to explore developing immunology disciplines such as immunogenomics, proteomics, and signaling. For more on Finn, see page 30 profile.



Gorin

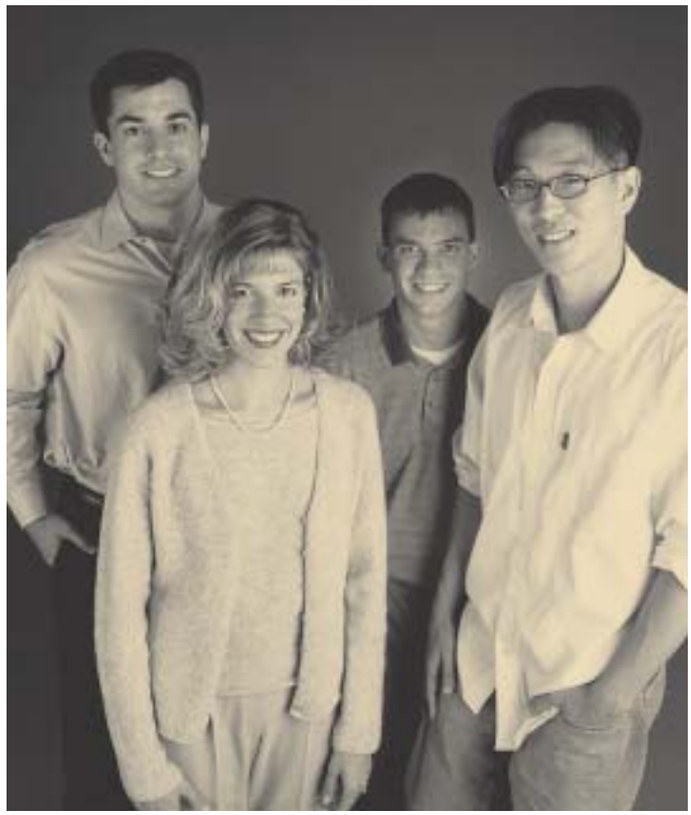
**Michael Gorin**, professor of ophthalmology, was recently named acting chair of the Department of Ophthalmology after serving more than three years as interim chair of the Department of Human Genetics for the Graduate School of Public Health. He plans to expand the department's research efforts in the following areas: diabetic retinopathy, corneal engineering (the creation of an artificial cornea), and gene therapy for the treatment of eye diseases of the retina and the cornea. To read about Gorin's own work, see page 8. —*DH*

## FLASHBACK

**On September 11, Steve King, MD '01, headed to Ground Zero to help at impromptu triage areas. But like so many others, King, an emergency medicine resident at Beth Israel Medical Center, found no one to mend. The injured never arrived. He and the rest of New York were met instead by a flurry of paper. That ate away at him. Millions of printed e-mails, memos, contracts, remnants of lives, limped downward to rest in pools of water and piles of concrete dust or stumbled into backyards in Brooklyn. But these belonged in desks, briefcases, filing cabinets; never were they meant to be ripped loose to flail in the wind.**

# SMELL THE ROSES AND ACE THE EXAMS

MOST WANTED STUDY PARTNERS | BY JENNIFER LEE



PATRICIA NAGLE

FROM LEFT: **Madder, Brandt, Golob, and Park nabbed the Class of 2004's basic science excellence awards.**

At the Omni William Penn Hotel in downtown Pittsburgh, polite company pour cream or squeeze slices of lemon into cups of hot, dark tea. A young woman plays a grand piano; Gershwin songs punctuate the afternoon's conversations, accompanying the clink of spoons set down onto saucers. The patrons, who stop occasionally to listen between sips, might recognize the pianist. Maybe they heard her playing at Lucca on a Saturday night as they dipped slices of bread into olive oil and someone sang show tunes. They probably do not know, however, that in her other life, Lynsey Brandt is a medical student. And it might never occur to them that playing the piano could help someone become a better doctor.

For Brandt, MD '04, performing is one way to balance the rigors of medical school. One of four students who earned a First Year Award for Excellence in the Basic Sciences, Brandt says she was terribly nervous about doing well at Pitt, "So I would study, study, study." Brandt, who is 25 and also holds a doctorate of pharmacy from Duquesne University, says she had to teach herself to relax, to not let the world pass her by:

"As physicians, we have to continue growing in all aspects of our lives. We have to experience the beauty of the world."

Brandt's fellow winners—Ryan Madder, Joe Golob, and Samuel Wan Park—likewise make real efforts to get away from their studies and rejuvenate. Park, 24, will admit, almost reluctantly, that he loves to play video games. *This doesn't seem very medical student-like,* his voice seems to say. Nor does reading all the Harry Potter books, something Park reveals in a similarly embarrassed tone. Park studied molecular and cell biology at the University of California, Berkeley before switching to economics because he thought it would offer him a deeper challenge. He says that before that he was a typical teenager, too cool to worry much about what he would be when he grew up. And medicine had left a bad taste in his mouth after seeing his brother fight off pituitary cancer. Somewhere along the way, he changed his mind about medicine—he's clearly inspired by its potential now and holes up on weekends cramming. One thing hasn't changed from those teenage days; Park is convinced there's nothing like a good game of, say, Starcraft for refueling.

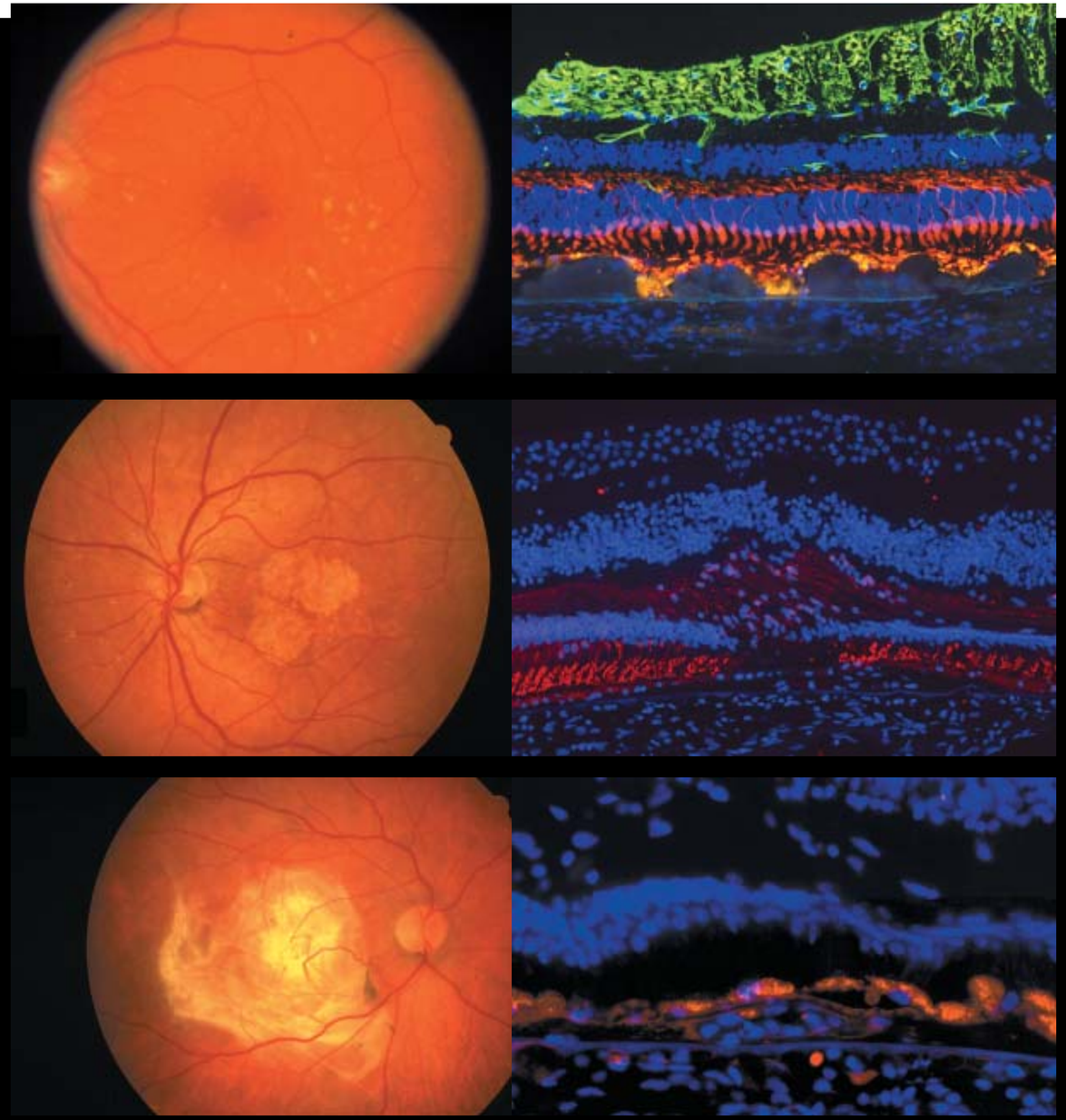
**Ernest Hemingway's stories appeal because the characters lead such relaxed lives.**

Madder, 24, who studied biochemistry at Swarthmore College in Pennsylvania, says Ernest Hemingway's stories appeal because the characters lead such relaxed lives. Finding time for leisure in his own story certainly isn't easy; at the same time he's not willing to neglect the challenge. "A lot of the way I study has to do with the fact that I'm married," Madder says. He'll be up at the crack of dawn to study before class, and often work through lunch so he can stop by dinnertime and spend the evening with his wife.

Golob, 25, thrives on early morning study sessions. Weekends are when he excels at unwinding. Whenever he can, he takes his boat out to compete in daylong bass fishing tournaments. After graduating from the University of South Carolina with degrees in biology and chemistry, Golob spent two years working in an artificial lung lab at what was then the McGowan Center for Artificial Organ Development. That's when he bought the boat, about the same time he applied to medical schools. (It took two rounds of applications before he was accepted, making this award especially sweet.) There's always some other school project for which he can prepare, but out on the river, with the light bouncing off the water, Golob's charge is just to sit and wait.

## FOOTNOTE

**So much for the good life. New Pitt MDs are paying an average of $2,200 every month just in student loan payments. On a resident's salary, there isn't much left for rent, car payments, day care, utilities. . . . (For more information or to help, call 877-MED-ALUM.)**



**TOP LEFT: Yellow spots in the eye are drusen, deposits found in many people with early age-related macular degeneration (AMD). TOP RIGHT: Detailed view of drusen. MIDDLE LEFT: Eye with "dry" AMD, the more common and less severe form of the disease. The yellow areas are blind spots caused when the pigment epithelial cells underneath the retina atrophy. MIDDLE RIGHT: Detailed view of the atrophied cells. BOTTOM LEFT: Eye with "wet" AMD, the more severe form of the disease. Yellow area is a blind spot caused by abnormally growing blood vessels that leak, triggering scarring. BOTTOM RIGHT: Detailed view of scarring. Sixty-five percent of the patients in the Pitt study had "wet" AMD; the rest had "dry" AMD.**

DR. ANN H. MILAM, SCHEIE EYE INSTITUTE, UNIVERSITY OF PENNSYLVANIA

# FOUND: MACULAR DEGENERATION GENES

**LOST: THE EARLY AND LATE-STAGE DISEASE LINK | BY TRINA WOOD**

The older man on the other end of the line sounded irritated. He asked Michael Gorin, then an ophthalmology resident at the University of California, Los Angeles, why he had failed to show up at an awards ceremony the previous evening to accept a prestigious honor. Gorin apologized and explained that he hadn't been notified to attend, then arranged to meet revered ophthalmologist Henry Nesburn, the voice on the phone and donor of the LA Ophthalmology Society's Henry and Lillian Nesburn Prize for Research.

When Gorin arrived at the great doctor's home 16 years ago, the first thing he noticed was the TV; the largest he'd ever seen. It wasn't that Nesburn wanted to catch every close-up during a football game, but that his eyesight had deteriorated to the point where a huge screen was necessary to watch anything. He was battling the advances of macular degeneration. The most common cause of vision loss in people over 60, age-related macular degeneration (AMD) damages the center of the eye's retina, placing a blind spot in one's field of vision. Although few people with AMD go blind, many of those affected can no longer engage in daily activities such as reading or driving that require sharp, central eyesight.

What impressed Gorin more than the big-screen TV was Nesburn's ability to lead a full, satisfying life despite his severe visual limitations. So began Gorin's fascination with AMD and a long friendship. "It's a good thing nobody ever told me about attending that evening," says Gorin, who is now interim chair of ophthalmology at the School of Medicine. "It's unlikely I'd have been inspired as I was just shaking Henry's hand at a podium."

Gorin's inspiration soon expanded to an exploration of the genetic influences of AMD, which afflicts more than 13 million Americans.

After more than a decade of compiling genetic data on 860 people from nearly 400 different families, Gorin and his colleagues, including Daniel Weeks, associate professor of human genetics, have now identified loci, or regions, on four separate chromosomes that appear to contribute to AMD susceptibility. The study, which appeared in the November 5 issue of the *American Journal of Ophthalmology,* suggests that regions on chromosomes 1 and 17 are most strongly linked to AMD; chromosomes 2 and 12 also appear to be somewhat involved.

Working with a late-onset disease presents a big challenge because genetic information from the parents of elderly patients is often unavailable. In hundreds of the cases in the AMD study, no blood samples existed from parents. So Weeks (who is the lead author on the November paper) had to determine their probable genotypes on the basis of offspring genotypes. Their study also took some wind out of a long-held hypothesis: that is, the same genes that contribute to juvenile macular dystrophies must also be major contributors to AMD. They probably aren't after all, says Gorin:

"We used to think that early onset disease and late-onset disease would simply reflect different variations in the same genes. However, our study suggests that this is only true for a very limited set of cases, and it is likely that different genes contribute to different forms of a disease." (These findings mirror studies by researchers comparing early and late-stage onset forms of complex genetic disorders such as Parkinson's and glaucoma, Gorin notes.)

Gorin is now interested in looking at additional families to verify their data and identify more precisely the genes involved in AMD. With that knowledge in hand, researchers could use genetic testing to identify high-risk individuals when they are asymptomatic. They would also be able to study how genes are regulated in order to develop therapies that might slow the progression of the disease. And that, in the long term, would mean ophthalmologists could test therapies to see if the risk of vision loss can be minimized.

In the next five to 10 years, Gorin hopes to collect enough data to conduct an interventional clinical trial with people known to be at high risk for AMD. "That's where genetic testing is of real value—in the preventive approach," he says. ■

## DO THE NUMBERS

**"I like biology, but discovered that in the lab I drop things," says Daniel Weeks, looking back on how he ended up as a statistical geneticist. Humility aside, Weeks is clearly no bungler. The 40-year-old chief of Pitt's Division of Statistical Genetics was singled out this year by the American Public Health Association with the highest honor it bestows on young health statisticians. Weeks makes complex genetic disorders more palpable to researchers at Pitt and throughout the world. His collaborators note they wouldn't even consider taking on huge, dense studies—such as pinpointing the genes responsible for age-related macular degeneration—without knowing they'll have guidance from the likes of Weeks and colleagues. His division's core faculty members include Eleanor Feingold, Candace Kammerer, M. Michael Barmada, and Jeff O'Connell. Their forte is making an analysis run smoother and faster as well as reveal more. For example, O'Connell and Weeks made one algorithm run, oh, 7,000 times faster than anyone had before. And almost every paper to come out in the past few years that analyzes family linkages in genetic disorders uses a program that O'Connell wrote to check mistakes that might have been made in labeling genotypes. The division has licensed the program for commercial interests. "One biotech company with 40 programmers just bought it," says Weeks. "We have one programmer. That makes me feel pretty good." *—EL***



Frymoyer

ERICA LLOYD

# UP CLOSE

**AMONG THE FIRST DORIS DUKE CLINICAL RESEARCH FELLOWS | BY ERICA LLOYD**

South of San Francisco, off the reef from a town that carries the curious name, Princeton-by-the-Sea, that's where you'll find *the* big wave break: Maverick's. There, a confined subset of Type As take on 50-degree Fahrenheit water, jagged rocks, shifting currents, and 60-foot-high wave faces funneling into booming tunnels of frothy gray energy. Nature is glorious yet belligerent in these waters. In the past decade, Maverick's has killed one professional big-wave surfer and injured a few others.

So when Adam Frymoyer, who is new to Northern California and new to catching waves, says, "Have you ever heard of Maverick's?" it's fair to wonder—*he's not really saying he surfs that break?*

No, no, no. Frymoyer doesn't surf Maverick's. He is just learning to get up on a board. He is a sensible person. He would, however, like to get a look at those monster waves. But it's a good idea to check with Frymoyer, MD '04. It's *not* misreading him to take him for someone determined to get the most out of every experience. The 24-year-old Harrisburg native is spending what would have been his third year at the University of Pittsburgh School of Medicine instead as a Doris Duke Clinical Research Fellow at the University of California, San Francisco (UCSF). Fellows receive a $20,000 stipend and a chance to learn the ins and outs of clinical research at one of the Doris Duke Foundation's six program sites. This is the first year of the program.

Frymoyer landed in San Francisco in July; by September he was finishing up UCSF's Training in Clinical Research coursework. The program is usually only undertaken by MDs who've finished their residencies. (Pitt has a similar program that awards a master's degree.) He dove right in, soaking up all he could about ethics, execution, and presentation of clinical research. Now he's pursuing advanced classes in statistics and epidemiology—and anything else he can fit into his schedule. Most of his energy is put toward moving forward clinical trials at various stages of development within UCSF's Pain Clinical Research Center.

"What sensitization means is this nerve fiber is more reactive, so its threshold to pain is changed." Frymoyer describes how he creates sensitized pain regions in healthy volunteers. He uses a "heat cap" method, so called because it employs a combination of topical capsaicin and heat. The idea is to mimic the experiences of chronic pain sufferers. Frymoyer's enthusiasm for the project makes one consider signing up, even though the intended end for the trial volunteer is straightforward: Pain. For a little while anyway.

He is able—temporarily and gently, at the level of a first-degree burn—to get a nervous system to respond in much the same way it would complicate the life of someone suffering from, say, postherpetic neuralgia (the pain some people continue to experience years after a shingles attack). One of the phenomena he's able to mimic is known as allodynia—which can make a seemingly harmless stimulus, like the grazing of a shirt, actually hurt. He softly takes a brush to an arm to demonstrate: "If I rub with this brush, it just feels like a brush, right? It's not painful. After this heat cap model, if I rubbed you then, it would become painful, unpleasant."

His UCSF mentors, Michael Rowbotham and Karin Petersen, developed the model as a way to determine the effectiveness of new analgesics before proceeding to more costly and complicated trials. Using the model, Frymoyer is testing a compound for a pharmaceutical company. He's helping with other trials as well.

This isn't Frymoyer's first immersion in research. He spent the summer of 2000 as a fellow of the American Pediatrics Society—a good experience. Still that was only eight weeks. "I wanted to fit clinical research into my future," says Frymoyer. "I wanted to have the proper background and training. Something to go on." At the end of his second year in med school, he told himself it was now or never. He wanted to do a year of research without interrupting his third and fourth year rotations.

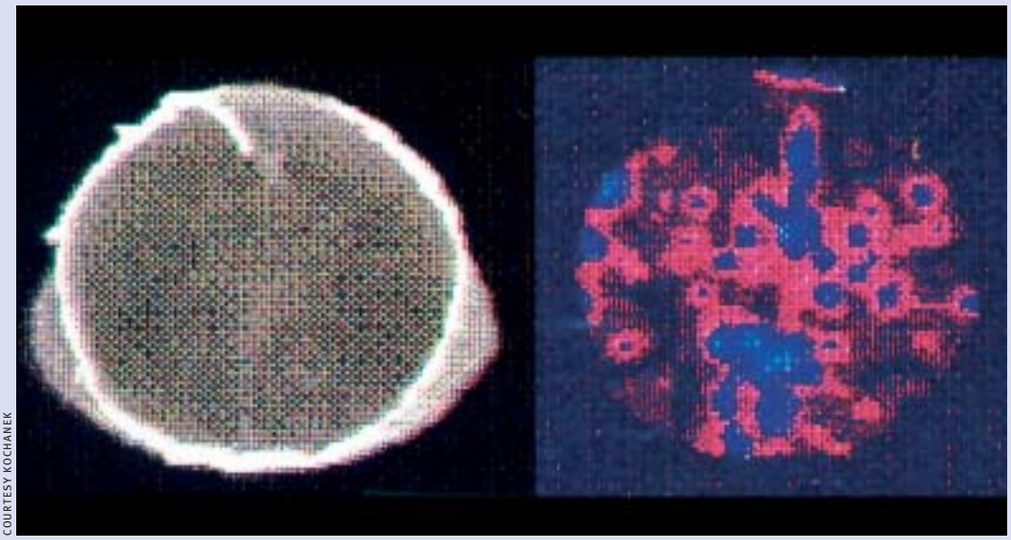
Now he is seeing the life of a clinical researcher up close. Rowbotham, who happens to be an avid surfer, takes him on rounds. (He also has offered to take him to some nice breaks. Frymoyer wants to make sure he can stay up on the board for a while before he puts himself on the spot with his boss, though.)

This fellowship has been exactly what he hoped for, and more. Frymoyer doesn't even mind all the paperwork for internal review boards and state advisory panels. That's part of protecting human subjects, he'll say. He just wants to make sure he knows exactly what to expect when he's an MD running trials himself. ■

# CLUES TO CHILD ABUSE

## BRAIN DAMAGE THAT'S BIOLOGICALLY DISTINCTIVE

BY JENNIFER LEE AND DOTTIE HORN



COURTESY KOCHANEK

**This cerebral blood flow map is from a month-old infant who has suffered severe head trauma as a result of child abuse. The map shows that the infant has very low blood flow to the brain. The inadequate blood flow increases the brain's susceptibility to damage.**

Sometimes, brain damage hides. It's not unusual for pediatricians in their clinics to examine children who "just don't look right." Maybe a toddler is irritable, colicky, or her color is off—that can mean cerebral damage, but there's no clear evidence. In such cases, it can be difficult to justify a CT scan, which is often revealing. The work of Pitt MDs Patrick Kochanek and Rachel Berger is likely to help such diagnoses. Berger is one of several faculty and fellows working with Kochanek to give the medical community an understanding of the damaged brain at a new level. Kochanek, a professor of anesthesiology, critical care medicine, and pediatrics, is hopeful these studies will lead to, among other advances, a blood test that can pick up biological markers of damage. The work may even offer new ways for physicians to identify cases of abuse.

This is an outcome Kochanek wouldn't have predicted. "The child abuse angle came out of the woodwork," he says.

If a child suffers from severe head trauma, from a car accident, for example, the brain tissue swells, and pressure builds inside the skull. As the pressure grows, it becomes harder and harder for blood to flow through the vessels in the brain. Hours later, the child is likely to be comatose and on a respirator. Neurosurgeons like Kochanek's colleague David Adelson may drain cerebrospinal fluid (CSF) in order to relieve some intracranial pressure. CSF is a clear fluid that continuously percolates around the brain.

In most cases when CSF is drained, the fluid is thrown away. But, seven years ago, Kochanek decided to begin collecting and studying CSF from pediatric cases. Other researchers had studied the fluid, but Kochanek wanted to submit it to a more extensive battery of tests. Few had studied CSF from children. Kochanek began collecting samples and, soon after, initiated a pediatric CSF bank, which is now funded by the Centers for Disease Control and Prevention.

In a freezer housed in the Safar Center for Resuscitation Research, which Kochanek directs, sits a collection of about 1,000 samples of CSF gathered from about 100 infants and other children. In most cases, samples were taken sequentially from patients, to allow scientists to study changes over time.

When Kochanek began studying the samples, he set out to understand better, at the molecular and biochemical levels, how a brain is injured by trauma. He explains that there are two phases of injury. There's primary injury—the impact itself—which destroys a certain number of neurons. But the majority of brain damage occurs from secondary injury—neuron damage in the region surrounding the site of the impact, which takes place in the hours and days following the impact. Kochanek focused on mechanisms of secondary injury.

In so doing, he discovered that child abuse victims stood out as a very distinct subpopulation within his group of severe head trauma victims. Their glutamate levels, for example, were off the chart. Glutamate is an excitatory neurotransmitter, essential to cognition in a healthy brain. The victims of accidents had elevated glutamate levels. Known victims of child abuse—who suffered head trauma from being shaken, from having their head hit against a wall or other object, or from blows to the head—had glutamate levels that were several times higher than levels in accident victims. A high level of glutamate in the brain, in combination with the low blood flow that results from the high intracranial pressure, creates seizure-like conditions. Kochanek believes this condition is one mechanism for secondary injury of brain tissue.

Collaborator Robert B. Clark, of the anesthesiology department, came across another biological tattler. Cytochrome C is a protein found in the mitochondria and plays an important role in normal cell function. When released into the cytoplasm, however, it triggers cell death. Clark tested CSF for cytochrome C and found it in only two subpopulations of severe head trauma victims—those who died and child abuse victims. This suggests that the brains of child abuse victims are more severely injured than those of accident victims, and that they are injured in a qualitatively different way. The differences could be caused by many factors, including the multiple injuries abused children often suffer and the delay in treatment typical among victims of abuse. ■




What, besides Mylar, has made Scope and Scalpel sparkle for so long? (Shown here, the 1969 *Medic Hair* production program cover.)





WHY THE SHOW MUST GO ON

BY SALLY ANN FLECKER

# GIVE MY GRAND ROUNDS TO BROADWAY

Lois Pounds Oliver (MD ’65) still regrets the floating chickens. Not the floating chickens per se. The chickens were great at the Saturday night performance of *Coldfinger,* fluttering down so softly from the great catwalk above the stage in the Stephen Foster Memorial Theatre. In fact, those live chickens were practically a showstopper—not only for the surprised audience but also for the startled cast. The chickens descended at the close of the first act, during the “Womb at the Top” number (sung to the tune of “Milk and Honey”), a satirical homage to Magee-Womens Hospital. Those 17 men singing their hearts out, and done up as heavily pregnant women in blond wigs, had no clue that the show was about to take a fowl turn.



The idea to use poultry to ratchet up the silliness of the skit had come late in the game—after the show’s Friday-night performance. One of the stagehands, who grew up on a farm, remembered that if you dropped a chicken from on high it would flap its ineffectual wings and ease itself to the ground like a dandelion wisp caught in the breeze.






**FROM LEFT: *PMS IV* program cover; the first executive committee—(sitting, from left) thespians Miller, Prefett, Aronson, Swartz, Titchworth, Stuart, (from left, standing) Dodds, Wilson, Harrington, Lommen, Yelle, Eisler, Wintell, Jones, DeCenzo; rehearsal for *Spring Tonic* (1956).**

*Let's do it,* said his cohorts. Exit stage right. They conducted an impromptu casting call at a local farm and by show time the next evening had a cadre of hens waiting in the wings. Oliver's lament some 36 years later comes from the success of the coop coup: "We always wished we had had it at the end." The retired Oliver, who last served as an associate dean for Duke University, has a good point. After all, how do you follow a chicken?

The feathering of the Saturday night performance of Scope and Scalpel—the musical extravaganza written, produced, and performed each year by soon-to-graduate fourth-year medical students—was not the only last-minute addition to the 1965 production. Four nights before the opening, Oliver and her coproducer, Alan Tapper (MD '65, a Baltimore-based ob/gyn) came to a sinking realization. They didn't have an opening, at least not in the grand Scope and Scalpel tradition of big production numbers with the entire cast on stage. Oh, the wringing of hands and the gnashing of teeth! But from desperation was born brilliance.

Not for the first time, and certainly not for the last time in Scope and Scalpel history, the previous year's production, *Beyond the Syringe,* contained a line that proved deeply offensive to a faculty member. His complaint to the dean sparked the following caveat: The tradition could continue, but the dean would read the script beforehand. *Hmmm.* This was fuel for the fodder for the *Coldfinger* gang. On Friday night, when the curtains should have parted, the musical director strode somberly out onto the stage. He was very sorry, he told the audience, but the dean had read the script and found it unacceptable. In place of this year's play, Jim Allison (MD '65), a fine pianist, would perform a concert. A baby grand was wheeled out. Allison, elegant in white tie and tails, sat down to play the opening notes of Rachmaninoff's Piano Concerto no. 2.

Suddenly, the orchestra leader shot up in the third row and fired a blank at Allison, who collapsed across the keys with a dissonant clatter. As he and the piano were wheeled off stage, six men, looking ominous in stocking masks and all-black costumes, marched down the aisle and up onto the stage singing the show's opener to the tune of "Goldfinger." (The dean, by the way, had approved the script, although that protocol was soon abandoned.)

The *Coldfinger* crew had pulled it off. Their show started with a big "bang."

**The names still get a chuckle: "A Scar Is Born," "Days of Line and Hoses," and, of course, "From Here to Maternity."**

Speaking of the big bang, the Scope-and-Scalpel creation myth goes something like this. In 1955, back in the days when the school was a little smaller, a fourth-year medical student, one Sam Aronson (MD '55, now an ophthalmologist in San Francisco), was shooting the breeze with Frank Dixon, then the young chair of the pathology department (see profile, p. 26). Medical school was set up so that the students spent their first two years in lectures together, then dispersed for the last two years as they wound their way through clinical rotations. *Wouldn't it be great,* Dixon wondered aloud, *if we could think of some way to bring the class together?* The ensuing discussion is lost to posterity—not so its result: *Hey, kids! Let's put on a show!*

Aronson tested the idea out on a few friends, including Felix Miller (MD '55, today a retired ob/gyn), whom everyone calls by his enduring childhood nickname, Bebe. Miller would become the first show's musical director. That irony still makes him laugh. Seems he wasn't much of a singer, and since there was no score, he could only convey the music to the rehearsal pianist by arduously playing single notes with his pointer finger. Still the idea of a class play became a snowball rolling downhill. A committee was formed. By show time, 99 percent of the class had enlisted. They built sets and made costumes. They wrote skits that poked fun at the quirks of the professors and lampooned the vicissitudes of their four years of med school. They produced, directed, acted, sang, and danced. "It was the blind leading the blind," Miller remembers. But soon what started out as a few skits in the imaginations of Aronson, Miller, and company had turned into a two-hour musical review. *PMS IV*—taken from the designation for a fourth-year Pitt medical student—looked superstition straight in the face. It debuted in May 1955, on Friday the 13th. The date did not prove unlucky. This year, when the Class of 2002 stages their musical, it will be the 48th consecutive Scope and Scalpel production.

But it is Ross Musgrave (MD '43 and executive director of Pitt's Medical Alumni Association) who should be credited with keeping the momentum going. He served as faculty adviser that first year. *PMS IV*'s program notes include this cheerful "postscriptum": *To our successors, to all future PMS IV's; we offer simple advice. Give it a try!* So that fall, Musgrave laid down the gauntlet at the feet of the Class of '56.

"You've been given this challenge by your predecessors," he told them at an assembly in the Mercy Hospital amphitheater. "I hope you'll take them up on it, and I would be happy to work with you on it." Almost immediately a group came forward who would meet at Musgrave's Highland Park home in the evenings.

"They'd sit on the floor and thrash out ideas on how they were going to do the show," Musgrave, who would also advise the next six





**FROM LEFT: *Nary a Golden Apple* producer Bert O'Malley, MD '63; angels from 2001's *Sixth Stench,* including lead, Alia Matthews, MD '01 (front row, second from left); *Anal Powers* lead John Whiteford, MD '00**

classes, recalls. "That show became *Spring Tonic.* The program was a far cry from the previous one. It had advertising, thick paper, and included the words to the songs. Instead of original music, they used show tunes, pop tunes, and changed the words." Another legacy of the 1956 production was the name—Scope and Scalpel—coined by the show's director/producer Cyril Wecht (MD '56), the now-legendary Allegheny County coroner.

The best skits were the ones that found the exact confluence of the times, the medical profession, and the idiosyncrasies of beloved—and not-so-beloved—faculty. There was, for instance, a between-scenes video, produced for *Jerry MaGuaiac* (1998) in the tradition of *Saturday Night Live,* featuring the soon-to-retire biochem professor Carol Coffee. The video shows Coffee matter-of-factly helping students above and beyond the call of duty—carrying books for one struggling with a stack higher than her head, changing a flat tire on the street for another. . . . And the skit that spoofed *The Exorcist,* showcasing pediatrics attending Basil Zitelli (MD '71)—well known for coediting the *Atlas in Pediatrics Physical Diagnosis*—who has seen more than his share of unusual cases. In the skit, Zitelli teaches a medical student the art of conducting a physical exam on a child who can levitate, turn green, and swivel his head 360 degrees.

One year, the two young sons of Bebe Miller were shot out of a cannon. Miller, by the way, stepped up to the plate as faculty adviser when Musgrave stepped down. (Miller's son Andy, MD '91, survived being shot out of a cannon and, years later, codirected the Class of '91's production, *Phantom of the OR.* Today he's in Boston, at Brigham and Women's Hospital.)

"Bebe is the producer type, a razz-matazzer." says Richard Moriarty (MD '66, the pediatrician of "Mr. Yuk" fame), whose own Scope and Scalpel was *The Sordid Life of Wally Pimpstein.* Moriarty, to whom Miller handed the faculty-adviser baton in the early '70s, describes himself as a nuts-and-bolts guy:

"I like to *do* the show—the scenery and the lighting and that kind of stuff. Everyone kids me that the finales were spectacular when I did the shows because I used every ounce of Mylar that was ever made."

Truth is, what jazzed Moriarty even more than Mylar was the opportunity for pyrotechnics. Every year he tried to convince the writers to work a volcano into one of the scenes. One year, to his delight, they finally did. "And it worked!" he reports with glee.

The year of the volcano was 1985; the show, *Lost in Scaife.* Director Sue Dunmire (MD '85) and music director Sam Tisherman (MD '85) were married the Thursday after the show. Their production also started with a big bang. The plan was that a big black obelisk would rise up from the stage in a cloud of smoke. Once it was straight up, fireworks were to be set off and the band would play *Also Sprach Zarathustra,* a.k.a. the *2001: A Space Odyssey* theme. The thing is, the producer was concerned about having enough smoke, so he rented extra-heavy-duty smoke machines. "The lights were down, and the band started playing," says Tisherman. So far, so good. But then the curtains went up, and all the smoke came down right onto the band. "I'm trying to direct the band," says Tisherman, "but we couldn't see each other."

Could it get worse? Yes. After infiltrating the band pit, the smoke floated into the auditorium and buried the entire audience. Dunmire and Tisherman (who are now associate professors of emergency medicine and critical care medicine, respectively) jointly took on the job of faculty adviser in 1991. They report that productions have taken a turn for the "less elaborate."

The content of some skits may be long forgotten, but the names still get a chuckle: "A Scar Is Born," "Days of Line and Hoses," and, of course, "From Here to Maternity." And the songs: "This Gland Is Your Gland," "Like a Surgeon," "Are You Going to Student Affairs," "Fifty Ways to Leave Your Liver," and the perennial favorite, "Thanks for the Mammary."

Why has Scope and Scalpel persisted after all these years, through all of the changes in the world? "It's a big release for a lot of people," says Aaron Bornstein (MD '99), a pediatrician at Children's Memorial Hospital in Chicago, who cowrote and produced 1999's *Saving Ryan's Privates.*

"Students see it as a way of getting things off their chest—good, bad, and indifferent," observes Moriarty. "The students say pretty truthful things. What they wind up saying is important to say. That's why the Golden Apple is a part of the show, and the Anus Equinus. It's the yin and the yang." [The Golden Apple recognizes the profs likely to save students' tushes; Anus Equinus recognizes those who are themselves horses' asses.]

Through the Mylar and smoke machines, students recognize each other in new ways as well. "Every year you see quiet students who have not bonded yet with the class," says Dunmire. "And then they come up on stage, and the class begins to see what they can do. They gain a whole new respect in the eyes of their classmates."

## And the songs: "This Gland Is Your Gland," "Like a Surgeon," . . .

"Medical students have talent coming out of the ears," says Moriarty. "But those other talents aren't recognized at all.

"No one is going to say, 'Oh, by the way, can you also play piano as well as do this presentation?' 'Can you tap dance as well as describe some disease entity?'

"In medicine you work hard together. You have to trust your colleagues; you become lifelong friends. The show does the same thing. It throws them into this thing that they suddenly realize they have committed themselves to do, and they will do the best that they possibly can. There's this magic about it."

And so the show goes on. What better way to wrap up four years of medical school than by leaving an audience in stitches? ■

A FAMILY GET-TOGETHER TO FIGHT HEREDITARY PANCREATITIS | BY DOTTIE HORN

# A MEMORIAL DAY TO REMEMBER

David Whitcomb had heard the stories of desperation. One woman had two children, 9 and 11, with hereditary pancreatitis, a little known disease. According to their pediatrician, either gallstones or alcoholism caused pancreatitis. The children clearly didn't have gallstones, so the doctor made a diagnosis that was heartbreaking but that logic seemed to dictate: "Her pediatrician told her that the reason the kids had pancreatitis is that they were sneaking out and drinking," says Whitcomb. "As a mom, she would see her kids rolled up in pain, vomiting and vomiting, and just crying out for help. These episodes would last for two or three days. What is she going to do?"

Whitcomb, professor of medicine, of cell biology and physiology, and of human genetics at the University of Pittsburgh, knew that the children were not closet alcoholics. Their disease was hereditary; in 1996, he had discovered a gene that caused it. A year later, as he planned the First International Conference on Hereditary Pancreatitis, he wanted the physicians and scientists who attended to hear stories, like the many he had heard,

PHOTOGRAPH | VICKY KASALA/THE IMAGE BANK

David Whitcomb has told the world more about pancreatitis than anyone has in probably 100 years. His breakthrough came thanks to a family reunion in rural Kentucky.

about living with the illness. He asked two people with hereditary pancreatitis to speak at the scientific meeting.

One of these speakers was Jean Burke (not her real name), whom Whitcomb had visited at home as part of his research. He sat in the audience as Burke told her story to a perfectly silent room:

*From the moment my daughter was born, I felt a deep tear in my heart that she would develop pancreatitis. . . . Last March, the inevitable finally happened when we learned she had this disease. . . .*

*She is five years old, she has blond hair, brown eyes, and she is filled with endless energy. . . . When she is sick, she will always have a stomachache, which terrifies her. It is this disease that she has that scares her. Lately, I have been able to tell her, "Do you remember those wonderful doctors who came out to the house and we met? Well, they are working on something to make you feel better. They are going to help us. They are doing their best." That helps her, she calms down, and she smiles.*

As Burke talked, Whitcomb glanced over his shoulder. In the audience, he recognized people who worked in his own lab or the labs of his collaborators. These researchers had no patient contact though, day in and day out, they moved the study forward. At some point, they may have held a vial of blood from Burke or another study participant. More likely, they'd seen only a minuscule amount of a clear solution derived from blood. Now they had a face and a story associated with the disease. Hearing Burke, it hit home: The hundreds of samples were from hundreds who were suffering and hoping.

Some of Whitcomb's colleagues had tears in their eyes. Others had tears streaming down their faces.

There was a time when Whitcomb could never have imagined that the thought of his work would someday help sustain a little girl through attacks of dreaded abdominal pain. Or that his first conference would inspire a sense of urgency in researchers working to better understand her disease. In the summer of 1975, Whitcomb was 20 years old, six-foot three-inches tall, with long, thick, blond hair. He combed his hair once every day, but only once, and drove around in a convertible, so his locks were usually tangled and windblown. He had just completed his sophomore year at Grace College and Seminary, in Winona Lake, Indiana, where he grew up.

In Winona Lake, Whitcomb spent summers baling hay on farms and taking advantage of a few of the 97 lakes in his county. Summer days were often filled with water-skiing, boating, fishing, swimming, hiking, hunting. One summer, wanderlust hit the teenaged Whitcomb, so he headed to Colorado: "I was hoping to herd longhorn steer, and I ended up hoeing sugar beets, among other things." He decided to go to college because he didn't know what else to do. In his first two years at Grace College, Whitcomb switched majors three times—it was history, then business, then art.

But art wasn't right either, and wanderlust had struck again. Whitcomb decided not to go back to school in the fall. A new plan emerged: He would buy a sailboat with a group of friends and spend a couple of years sailing around the world.

Then he started getting phone calls—sometimes at home, sometimes at work. The calls were from Richard Jeffreys, a professor of biology at Grace College. Jeffreys had a reputation at the school—most of his students made Cs, Ds, or Fs. Whitcomb, however, had aced his animal biology class the previous semester. The prof had heard that his star student was going to postpone college. *I'll be teaching anatomy and physiology in the fall,* Jeffreys said. *I'm designing the course with you in mind. If you don't take the course, it isn't going to be worth teaching.* After a few phone calls, Jeffreys won.

**"When she is sick, she will always have a stomachache, which terrifies her."**

It was the only course he took that fall. "After about three weeks, I couldn't put my textbook down," says Whitcomb. "I just loved physiology. I loved studying how vision works, how nerve impulses travel. Every part of the way the human body works is so perfect and cool that it's just amazing."

The sailing trip never materialized, but that was okay. By the spring semester, he was intent on raising his GPA and taking the courses he needed to get into medical school and a PhD program in physiology.

Sixteen years later, Whitcomb was a new assistant professor at Pitt. He'd received both an MD and PhD from Ohio State University, then did a residency in internal medicine and a fellowship in gastroenterology at Duke University. In graduate school, he studied the physiology of the pancreas. At Pitt he intended to continue that work; he'd also become interested in pancreatitis.

The pancreas produces enzymes that digest food; they are part of a juice secreted into the small intestine. Normally, the enzymes only become active once they are inside the small intestine; in the pancreas, they don't do much. In cases of pancreatitis, however, the enzymes begin digesting the organ itself. The result is more than just abdominal pain. Immune cells respond with an attack so powerful (directed against the pancreatic tissue) that patients can be hospitalized for months and sometimes die.

Little else was known about this mysterious disease when Whitcomb came to Pitt in 1991. No one knew, for example, how the digestive enzymes became activated prematurely—not until Whitcomb started looking into it.

He had an idea. He knew of a few, scattered published reports documenting cases where pancreatitis ran in families. The straightforward inheritance pattern indicated that a single gene was causing the disease. If he could locate the gene, he thought he could also locate the protein, encoded by the gene, whose malfunctioning causes the disease. (Other researchers, notably Nancy Wexler with her Huntington's disease studies, have successfully enriched understanding of hereditary disorders by focusing on afflicted families.)

Then, by looking at how the protein functioned in its normal and mutated states, he hoped to understand the cause of pancreatitis.

"Genetics was the only way that we could imagine to solve this problem," says Whitcomb.

As far as he knew, he had never seen a patient with hereditary pancreatitis. (Its clinical presentation is identical to that of other types of pancreatitis.) But he had heard that there was a family in Kentucky with the disease. A friend of his, Larry Gates, had a practice there. He called him, but Gates hadn't come across anyone with hereditary pancreatitis.

Two weeks later, he got a phone call from Gates: "Dave, you won't believe what happened!" Someone had just walked into Gates' office and declared, "I have hereditary pancreatitis."

"How do you know?" Gates asked.

The man took out a scroll and unrolled his family tree, with about 500 people mapped on it.

TOM ALTANEY



**As a researcher and as a community member, Whitcomb finds that outreach comes naturally to him. Here, he's shown at home with his "gigantic family," which includes young adults from his church who stop by each week.**

The generations dated back to the Civil War, so did the mysterious abdominal pain.

"Where do all these people live?" Gates asked.

They lived in the surrounding region, and the man was interested in participating in a study to help find the cause of the disease.

Whitcomb called up Gates' patient. *It's coming up Memorial Day,* Whitcomb said. *Why don't we have a family reunion and invite everybody?*

Whitcomb, a colleague, and two of his four children headed to Kentucky on Memorial Day, 1995, their car loaded with supplies needed to draw blood. His collaborators from Lexington and Cincinnati brought grills, meat, buns, and the fixings. About 140 people from the invited family came. In between helpings, Whitcomb's team charted the family history, listened to people's stories about living with the illness, and collected blood from nearly 100 people.

After his return to Pitt, Whitcomb's lab studied DNA from the blood samples. Within a year, they had discovered the gene that was mutated in the family members who had the disease. The gene, located on chromosome seven, coded for trypsin.

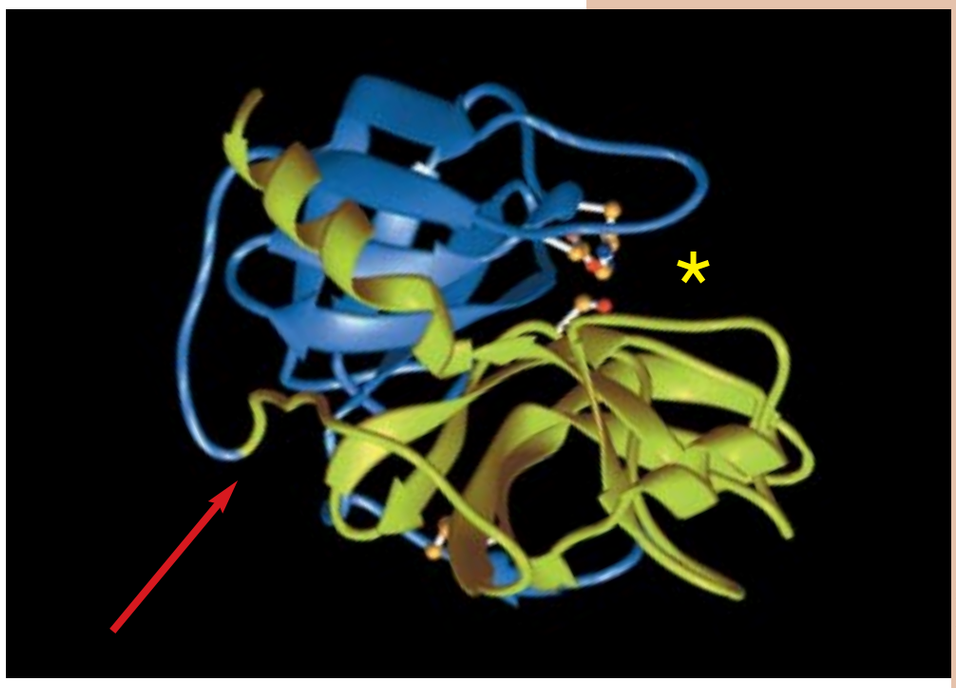
The pancreas produces about 30 important digestive enzymes, and among these trypsin plays a central role. Trypsinogen (the inactive form of trypsin) becomes activated when it touches the wall of the small intestine. Trypsin then sets to work—going to all the other digestive enzymes, converting the inactive form into the active one.

In everyone, trypsin sometimes becomes accidentally activated in the pancreas. If it does, a protective enzyme goes into action. The molecular structure of trypsin is such that there are two parts linked by a connecting chain. The protective enzyme simply cuts the

chain, disabling the trypsin. In the people Whitcomb studied with hereditary pancreatitis, he discovered the chain is mutated, and the protective enzyme is powerless to cut it. There is no way to shut off the accidentally activated trypsin. The trypsin activates all the other digestive enzymes, and they set about breaking down the pancreatic tissue.

Before this finding, the last major breakthrough in pancreatitis had been 100 years earlier, the 1896 discovery that autodigestion caused the disease rather than infection. Whitcomb had pinpointed a precise cause. The study was published in *Nature Genetics* on October 14, 1996. He had the first page of the article framed; it hangs beside his office door, where his eyes fall on it every time he leaves the office.

Since the 1996 discovery, Whitcomb has sought out other families with hereditary pancreatitis and has attended other family reunions. (It was on such an occasion that he visited Jean Burke's home.) To date, he has studied 746 people from 180 families with hereditary pancreatitis. His research has shown that not everyone with hereditary pancreatitis has the mutation he discovered in 1996. He discovered other mutations of the same trypsin gene that are linked to hereditary pancreatitis. Some of the families in his studies have the first mutation, some of the families have others, but some have no known mutation, so there is at least one other, as yet unknown, mutation that can cause the disease. Whitcomb is now trying to find it.




COURTESY FUREY

**An enzyme can inactivate trypsin by cutting the chain that connects the two parts of the trypsin molecule. In some people with hereditary pancreatitis, Whitcomb found, the chain is mutated, and the enzyme is powerless to disable the molecule. (Red arrow above points to chain.) Trypsin has also been implicated in nonhereditary forms of pancreatitis. Yellow star shows active enzyme site.**

## By studying the inherited disease, Whitcomb uncovered a mechanism important in all forms of pancreatitis.

His discoveries have implications far beyond the 1,000 to 2,000 people in the United States with hereditary pancreatitis. By studying the inherited disease, Whitcomb uncovered a mechanism (trypsin activation) important in all forms of pancreatitis. One percent of the US population is affected by pancreatitis or pancreatic cancer (which is often associated with pancreatitis).

Memorial Day 1996: Whitcomb was back in Kentucky, hosting a second reunion for the family he'd met the year before. He returned to share research results, including his discovery of the gene.

Whitcomb continues to keep the family informed. He publishes a newsletter called *Hereditary Pancreatitis Research News,* which is distributed primarily to participants in his studies. His outreach efforts also include his website devoted to pancreatic disease, http://www.pancreas.org. He receives about four e-mail messages a week from people with pancreatitis who have found his site. *Dear Dr. Whitcomb,* read one such message. *Hi, the Doctors think I have hereditary pancreatitis because my dad has it too. I don't really know much about it except that it hurts in your back, sides, and stomach areas (speaking from experience). I've been in the hospital for it once because it was the worst attack I've had. If you could send me more information on it, it would be greatly appreciated. By the way I'm 12, just in case it matters. . . . Have a nice day.*

Outreach seems to come naturally to Whitcomb, whether the circumstances are professional or personal. Every Wednesday, his family opens up its home to a few dozen young adults from his church.

"They like having a place where they can raid the refrigerator and lay on the floor and play with the dog," says Whitcomb. They're also likely to go to him or his wife with personal problems and questions. Some have nowhere else to turn, Whitcomb notes. "It's fun for us, because they're all our friends and they're like our kids. I have a gigantic family."

A few months ago, one of Whitcomb's collaborators mentioned that he had solved a problem that has puzzled scientists for generations, that is, how the pancreas is able to secrete sodium bicarbonate at the levels that it does. (Sodium bicarbonate is released into the small intestine, where it neutralizes the gastric acid produced by the stomach.) Whitcomb sat down that same afternoon to solve the problem for himself. "I thought, if he's smart enough to figure it out, I can figure it out," he says.

Hours later, Whitcomb had the answer. He called his friend back, only to find out there had been a misunderstanding. "Oh, no, that wasn't the problem we were working on," his friend said. But Whitcomb believes he has the answer to the ancient mystery, although he is awaiting scientific publication before he explains it to the rest of us.

He stops for a moment to reflect: "There's a proverb that I like. 'It is the glory of God to conceal a matter; it is the glory of kings to search out a matter.' There are things that have been hidden for eons past that nobody's understood. It is the privilege of kings to have the luxury to investigate what nobody's been able to figure out. What a job." ■

TRIAL VOLUNTEERS ARE THE HEROES OF CLINICAL RESEARCH | BY DAVID R. ELTZ

THE FIRST IN A SERIES

# TRIAL RUNS

Leslie "Butch" Levendosky never could wait around for life to come to him. He learned from his father, who worked hard, sometimes crawling on his belly, scraping coal from West Virginia mine shafts only 30 inches high. You do what you need to do.

Levendosky couldn't help but take that sense of purpose to Vietnam, and by the spring of 1969 he'd about had enough. One day the Viet Cong would shell the base with rockets, slip back into underground tunnels, and vanish into the 60 square miles of treacherous jungle above Saigon that made up the Iron Triangle. The next day Levendosky, a helicopter inspector, would find himself bored and imbibing the warm Miller he bought for $2 a case. Two months into his tour of duty, some 20

PORTRAITS | JIM JUDKIS

DUNCAN MCNICOL/STONE

of his 1st Cavalry unit's 27 helicopters had been shot down. It was enough to drive a man nuts. So Levendosky volunteered to lead search and rescue missions.

One day around Christmas, yet another helicopter went down, and Levendosky set out to find it. In a rescue helicopter above a jungle so often sprayed with Agent Orange that the carcinogen resembled a sheet of rain, Levendosky called back to his gunner. The guy was new in country, and Levendosky wanted him to know exactly what to do so no one on his team got killed. Above the cacophony of the chopper blades Levendosky shouted, "You're gonna have to put down ground fire to cover our butts!" The gunner nodded.

At the crash site, the Viet Cong were still firing from the tree line. The pilot put the helicopter down, the rescue team hit the ground, and the gunner pulled the trigger on his M-60. It jammed. Levendosky was still 50 yards from safety. With bullets zipping by, he ducked and ran, somehow making the tree line unscathed. Inside the jungle, the downed helicopter was mangled so badly it looked like a mashed Volkswagen beetle. The pilot and gunner were dead; the radioman was alive but dazed. Levendosky got the survivor out and called in commandos to blow up the helicopter so the enemy couldn't find salvage. A voice shot back over the radio: *No. The general, in Saigon, wants to see it. Bring it back.* Levendosky shook his head at the absurdity of it all and grabbed a cargo net to wrap around the wreckage.



**About 15 patients in the Pitt segment of a multicenter Phase I clinical trial for Gleevec will take increasing doses of the drug for up to eight months. Participants suffer from chronic myelogenous leukemia or another form of cancer; all have liver dysfunction. Dosages start at 200 milligrams a day and end at 800 milligrams a day. Investigators, led by Ramesh K. Ramanathan (above), want to establish maximum dosage levels for cancer patients with liver problems.**

"I got a Bronze Star for that," he says, chuckling from a hospital bed at UPMC Montefiore. He wears black jeans and a blue button-down shirt. Black wire-framed glasses snugly fit on the bridge of his nose. More than 30 years later, Levendosky is 56 and the manager of quality control for a pharmaceutical company. Time has turned his hair gray, his eyebrows bushy, and his colon and liver, and maybe now his lungs, into a factory of cancer cells.

A nurse will soon draw blood, to be tested for a protein that will indicate whether or not his damaged liver is processing the drug he has been taking for two weeks. The drug is so new no one knows how his body will respond to it. Levendosky is a volunteer for one of 3,000 human subject investigations conducted annually at the University of Pittsburgh, which range from psychology surveys to trials of new cancer drugs.

When the nurse comes, Levendosky tells her, "Tomorrow's the 31st [of October]. Dracula must be calling every half-hour and saying, 'I need a new shipment.'" His wife, Emily, calls him a "great role model" for other cancer patients. But the jokes come naturally to the soldier who rescued that dazed radioman in a place seemingly gone mad. He isn't about to wait around for death to get the upper hand just yet.

Dorothy Hank (not her real name) remembers that day on the Island of Patmos at the Monastery of St. John the Theologue, a medieval citadel built a thousand years earlier on the ruins of the ancient temple of the goddess Diana. It was 1995, and Hank was on a whirlwind tour of Greece.

She was at the souvenir booth, where she'd just purchased a $100 painting of the Virgin Mary and baby Jesus. Then she heard it—singing, so sweet. It was as if Mary herself, or even Diana, was calling out to her. Enchanted, she followed the voices to a nearby chamber, where she found a cluster of singing monks. She stopped to take in the mesmerizing tones. But not for long. A man in black rushed forward, exclaiming, "Excuse me. Ladies are not allowed."

Hank, at 5-foot, 2-inches, stood her ground. "I had gotten that far, and I came from the US, and I thought, 'I want to hear the singing; it's beautiful.'" And so she did.

Soon after, Hank, then 67, began feeling pain in her back. It would come when she stood up. "I'd go like this," she demonstrates, hunching her shoulders and grimacing, "because I was afraid." She sits in her spotless kitchen, her eyes swimming beneath thick trifocals as the mid-afternoon sun reaches across the table.

Hank was soon diagnosed with arthritis, and during a routine exam in 1998 her doctor told her she'd shrunk three inches. She wanted to be tested for osteoporosis. Hank insisted: "Two of my sisters have the disease; I want to be tested."

She was right; she had osteoporosis, a bone disease with no obvious symptoms (except shrinkage) that affects eight million women and two million men in America. One day she read a local newspaper advertisement about osteoporosis research at Pitt, picked up the phone, and dialed. By September 2000, she was enrolled in a study for a potential new therapy, just as confident in her decision as she was the day she refused to leave the singing monks.

Hank's decision to be a human test subject was important to more than her health. Clinical trials are the only way investigators can advance potential therapies from theory to everyday treatment. Without volunteers like Hank and Levendosky they wouldn't go forward.

"We're all either patients or potential patients, and what we want as patients is the best treatment," says Clifford Schold, head of Pitt's new Office of Clinical Research.

"Clinical trials are the way we get answers, the quickest way we get the most accurate answers. Everybody should want to participate in trials."

Levendosky returned home from Vietnam in 1970 and bought the car of his dreams, a 1969 Corvette Stingray. (He has it to

**"People say, 'Boy you got an attitude for cancer,' and I say, 'Well it don't bother me.' I've been through it all.**

this day.) Two years later he pulled his Triumph motorcycle into the garage, turned to his girl behind him, and said out of the blue, "Hey, want to get married?" They've been together ever since, and have reared two children. Levendosky also returned to his job as a bench chemist, often mixing with unprotected hands organic solvents like benzene that today are linked to cancer. Back then he and his buddies at work used to leave the lab saying, "Boy my liver's gonna swell by the time I'm 50." They were joking; no one knew then that such chemicals could be deadly.

It's more fun for Levendosky to talk about his hunting trips—like the time he went after big game with his brother in Canada in 1995. He remembers pulling the trigger to shoot a caribou, but his rifle, a Browning 300 Magnum, wouldn't fire. Cursing, he aimed in the air and fired again. Blam. Then he leveled the scope's crosshairs at the caribou and . . . click . . . nothing. He pointed at the sky . . . blam. At the caribou . . . click. At the sky . . . blam. Levendosky had failed to seat a trigger spring the last time he cleaned the weapon, leaving the rifle to fire only when aided by gravity. The next year the weapon—damaged after a horse slammed into the scabbard on his mount—fell apart as he fired at a bull elk in Colorado.

By April 1998, looking for a change of luck, he'd bought a stainless steel Ruger, preparing for a trip to Saskatchewan to hunt mountain goats. The trip was canceled. Doctors found a tumor the size of a "pack of cigarettes" in his colon.

Levendosky stops turning the pages of an album of pictures from his hunting trips. In a level voice he recalls the course of treatment that led him to this antiseptic-white room in Montefiore. Doctors did a resection of his colon. They removed his rectum. They found tumors in his liver and took out half of the organ. An ultrasound showed the cancer was gone. He underwent chemotherapy. Then, a CT scan found four more tumors, two on his inferior vena cava. Levendosky's doctor refused to touch this central vein, fearing Levendosky would bleed to death. Instead they put him back on chemotherapy. For two years.

He is quiet, staring at nothing in particular. As Levendosky recounts the last three years, one gets the impression that he has drifted off into one of his father's mines, the walls narrowing in around him until he's lying there beneath a 30-inch ceiling, and the only way out is the one he digs himself.

Finally, Levendosky looks up. In September a CT scan showed a tumor in his liver, he reports. A month later it had grown to five centimeters in diameter. There were spots on his lungs, too. Levendosky told his doctor: "I'd like to live a little longer."

The doctor enrolled him in a Phase I clinical trial for a new cancer drug called Gleevec. As it turns out, the trial is not designed to test a cure for his condition, though it could help. This treatment, in some respects, is a last resort. Levendosky accepts that: "If it helps somebody else, then I've done my job. I hope it helps me, but if it don't, it don't. At least [the doctors] will learn something from it."

Dorothy Hank is patient XXXX. An impersonal four-digit patient identifier marks the white plastic bottle sitting on her kitchen table, which holds pills that are either placebo or Fosamax. The drug Fosamax inhibits the work of osteoclasts, cells that excavate pits in the bone. After osteoclasts mine bone, another bone cell, an osteoblast, rebuilds new bone in the same place—ideally. Yet as we age, osteoblasts, the bone builders, can't keep up with osteoclasts, particularly women's. Often, women will lose 20 percent of their bone mass during menopause, much of the damage occurring in the hips and spine.

When osteoporosis sets in, the bones become porous and brittle. It is a silent process. Some women won't find out they have the disease until they fracture a hip. Then, it might be too late. More than 20 percent of hip fracture patients aged 50 and over die within a year of an accident. The process, fortunately, is preventable and partially reversible. Drugs like Fosamax can prevent bone loss. In this study, Susan Greenspan, MD and director of the Osteoporosis Prevention and Treatment Center at Pitt, postulates that the drug, in combination with a supplement of parathyroid hormone, could boost bone mass significantly.

## A CLINICAL TRIALS PRIMER

**At any given moment, there are roughly 3,000 active human research studies at the University of Pittsburgh. About 1,500 new studies begin each year. Some 470 of the ongoing studies at Pitt are biomedical, drug, and surgical device investigations—clinical trials that involve greater than "minimal risk" to participants. (The feds understand "minimal risk" to mean that the possibility of harm or discomfort during research is no greater than what is ordinarily encountered in everyday life.) Most trials at Pitt are in oncology, psychiatry, cardiovascular health, epidemiology, and women's health. What follows is the path most new treatments are routed through to become approved therapies:**

**• PHASE I**
**Investigators attempt to determine possible side effects as well as appropriate dosage levels, schedules, and routes (e.g., a medication might be better given through an IV rather than orally).**

**• PHASE II**
**Investigators test the efficacy of the drug against a particular disease.**

**• PHASE III**
**The drug is compared to the existing standard of care for the signal disease and related diseases, usually at a number of institutions running simultaneous investigations to gather a significant amount of data. The data is analyzed and published in a peer-reviewed journal. This is when new treatments are submitted to the Food and Drug Administration, which reviews the study results and might grant approval for therapeutic use.**

**• Passes Food and Drug Administration muster—**

**• PHASE IV**
**Investigators monitor a treatment's long-term effectiveness, its potential in combination with other modalities, its impact on quality of life, and its cost effectiveness.**

Clinical trials being what they are—research designed to find out whether or not something works—not even the nurses who record data about Hank know exactly what she's taking. Hence the impersonal "patient XXXX" printed on her bottle of pills. In the first year of this multicenter study, funded by the National Institutes of Health, each of the trial participants received Fosamax or the parathyroid hormone therapy or both. In the second year, which began in September, patients in three groups receive Fosamax; patients in group four get placebo.

Greenspan, principal investigator of the Phase III trial—the last step before a potential therapy receives a thumbs up or down from the Food and Drug Administration (FDA)—hopes to pinpoint any differences in bone-mass gain among the study groups. This will also tell her if the effects of the drugs last long enough so that women can stop taking them for a while.

**"Someone has to be in the program. If I didn't do it, who else would? There are a lot of people younger than me who need to know what to take."**

"I don't think as physicians we really think about what happens when women stop therapy," Greenspan says. "It's an important question." In short: Why continue to take a drug if you don't need to?



**Susan Greenspan (above) is running a study to determine a combination therapy's ability to reverse bone loss in osteoporosis. Under her direction, 73 patients in Pittsburgh will receive a combination of the federally approved drug Fosamax and a parathyroid hormone. Parathyroid hormone has not yet received approval from the Food and Drug Administration, but results from this Phase III study, which includes 240 participants at four centers, could change that. Dorothy Hank (shown far right) is in the second year of the two-year study.**

Every morning Levendosky takes 200 milligrams of Gleevec. Approved by the FDA in May to treat patients with chronic myelogenous leukemia (CML), it is the first of a new class of molecular targeting drugs. Gleevec is known to shut down a signaling protein called bcr-abl, which scientists believe causes CML. The protein is one of about 90 tyrosine kinases, and tyrosine kinases have been linked to many human cancers. In one study, Gleevec put CML into remission in 90 percent of participants. Not only that, but those patients experienced few side effects, since the therapy doesn't seem to destroy much healthy cell matter, unlike traditional chemotherapy. Essentially Gleevec is designed to jam signaling proteins, forcing cancer cells to trigger their self-destruct mechanism.

Ramesh K. Ramanathan, director of the Gastrointestinal Cancer Center at Pitt, saw the drug's potential, wondered if Gleevec blocked other tyrosine kinases, and offered the University of Pittsburgh Cancer Institute as the coordinating point for a 10-center trial sponsored by the National Cancer Institute. The eventual goal is to determine if Gleevec can treat other carcinomas, such as breast, lung, prostate, and colon cancers. But first, scientists want to learn if the livers of cancer patients with liver dysfunction can even process the drug, since so often cancer spreads to the liver. That's why Levendosky, who doesn't have CML, is eligible for the trial.

"We are looking to see how much of the drug stays in the blood, and for how long," Ramanathan says. Then, his team can begin to see if the drug inhibits the tyrosine kinase associated with colon cancer. "There's really little information available about how the drug is metabolized," the doctor explains.

Hank, now 73, learned recently that Ellen Roche, a healthy young volunteer in a trial at Johns Hopkins University, died in June after inhaling a chemical that caused her lungs and kidneys to fail. Roche's death led to a federal investigation that temporarily shut down most of the institution's 2,800 human subject trials and is likely to influence how research is conducted nationwide. But for Hank, that sad incident would not figure into her decision to be a human subject at Pitt.

"What's meant to be, will be. It's not going to hurt me," she says. "If I didn't do it, who else would? Someone has to be in the program. There are a lot of people out there younger than me who need to know what to take."

As for Levendosky, well, he made it through Vietnam. He worked his way up to management at the pharmaceutical company. He raised two children, one a National Merit Scholar, the other a clinical coordinator. He's not about to start blaming anyone for his cancer, or to slow down because of it.

"People say, 'Boy, you got an attitude for cancer,' and I say, 'Well, it don't bother me.' I've been through it all." What he means is that he's not finished yet. He has been thinking. He never has had a chance to hunt with that Ruger since he cancelled the mountain goat trip after his 1998 diagnosis. Maybe a visit to Saskatchewan with his brother will do him good. Maybe this year will be the perfect time. ■

*This is the first of a two-part series on clinical trials. In our April issue, readers will meet others who play quiet roles that lead to new therapies.*

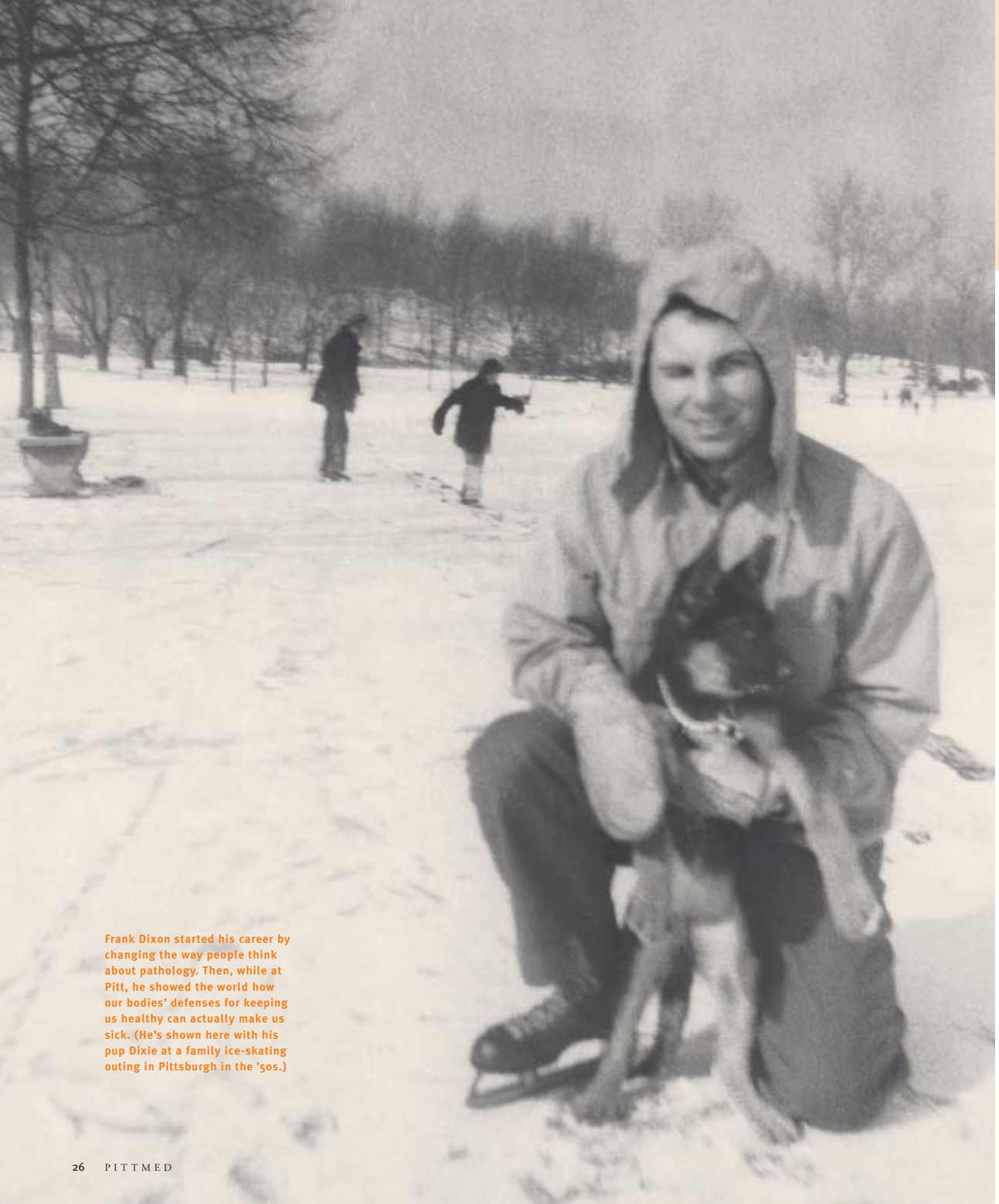
*As this magazine went to print, we learned that Leslie Levendosky's health took a turn for the worse. Our thoughts are with him and his family.*



**This woman is one of thousands of volunteers who make clinical investigations possible at Pitt. Dorothy Hank (not her real name) is participating in an osteoporosis trial.**

FRANK DIXON DREAMS IMMUNOPATHOLOGY AND WHITE SAND BEACHES | BY LEAH KAUFFMAN

# CALIFORNIA DREAMING



Frank Dixon started his career by changing the way people think about pathology. Then, while at Pitt, he showed the world how our bodies' defenses for keeping us healthy can actually make us sick. (He's shown here with his pup Dixie at a family ice-skating outing in Pittsburgh in the '50s.)

During a lunchtime football game near Pennsylvania Hall, young Frank Dixon cut a swath through the opposition. His build was average, yet strong from daily workouts, and he played with the determination of an all-American. Dixon's aggressiveness led to an escalation of the hits against him, which he met without complaint. Not everyone was able to keep his cool as the competition became bruising. One flustered medical student grabbed Dixon by the sweatshirt and let him know he didn't like his playing style. Dixon turned his piercing, blue-eyed gaze on his opponent, then shook him and the incident off easily. The game broke up as the lunch hour ended. At 1 p.m., the term's first pathology class convened. To the shock of all assembled, including the student who had threatened him on the field, in walked Frank Dixon, the new chair of the University of Pittsburgh School of Medicine's Department of Pathology, to lead the course.

Dixon was not long out of his own student days when a search committee led by Jonas Salk in 1951 tapped him to start a new research-oriented pathology program at Pitt, one of the first of its kind. He had a new tool to contribute to pathology, a way to track proteins as they moved through an organism. Salk must also have sensed the intangibles that his recruit brought to Pitt. The confident 31-year-old would later be named the nation's leading medical researcher under the age of 35 by the American Association for the Advancement of Science.

PHOTOGRAPHY | COURTESY MARION DIXON AND ROBERT E. LEE





**LEFT: Pitt became a center for immunopathology research. Shown here, faculty, fellows, and lab technicians in the Department of Pathology in the '50s. Dixon is in the second row, third from left. ABOVE: In 1975, Dixon surveys construction for a new building at Scripps on La Jolla's northern bluffs—not far from the Salk Institute.**

As a teenager, a restless Dixon left his hometown of Mankato, Minnesota. His parents, whose days were consumed running the family restaurant, had high expectations for their only child. Dixon yearned to see life elsewhere and find "somewhere in the world that's kinder to you than Minnesota." He glimpsed then that a spirit of adventure could pay off. After hitchhiking west, he and a high school friend happened upon the southern California seaside town of La Jolla. The temperate sea air was benevolent and beckoning compared with Mankato's extremes—its long months of short winter days and bitter cold, then stifling summertime heat and humidity. "La Jolla was about as good as you could do," Dixon thought; but he soon found himself back home, packing his parka to enroll in the bachelor of science program at the University of Minnesota in Minneapolis.

He thought he would pursue math as an undergrad, but was dissuaded by his adviser, a mathematician himself who didn't want Dixon to suffer the same poverty. Dixon chose medicine, then pathology, because he liked the idea of investigating a wide range of disease processes. After serving as a Navy lieutenant with the Marines (which lacked a medical corps of its own) during World War II, he went to Harvard University. There he worked with Shields Warren, a pathologist who would become the Atomic Energy Commission's first chief of the division of biology and medicine and an authority on radiation-induced disease. Because of Warren's connection to the AEC, Dixon had access to materials that were otherwise hard to get. Dixon applied a new technique for tagging proteins with radioactive iodine. He used this technique to follow proteins injected into lab animals, confirming their location and number with a Geiger counter, which reported the iodine's decay with disinterested accuracy. Pathology—which had been a science limited to observations of the microscope-aided human eye—suddenly became molecular and quantifiable.

At his first faculty position at Washington University in St. Louis, and then at Pitt, Dixon applied this new tool to one of immunology's oldest puzzles, serum sickness. Pathologists first came across serum sickness in the Preantibiotic Era, when the best hope for curing a nasty bacterial infection was to inject the patient with animal serum containing antibodies that targeted the bacteria. Those antibodies would lick the bacterial infection, but the serum exacted payment, typically in the form of fever, an enlarged spleen, joint pain, and rashes. Because these symptoms are so similar to human diseases like rheumatoid arthritis, rheumatic fever, and lupus, serum sickness induced in experimental animals is a good model of human immunologic disease. To the pathologist, the symptoms are most visible in lesions in the heart, blood vessels, joints, and kidneys.

It was already known that antibodies, seeing the proteins or antigens in serum as foreign, latched onto them to form so-called antigen-antibody complexes, but it was unclear what those complexes had to do with serum sickness. Dixon tagged the antigens with radioactive iodine and saw that they were circulating in the blood during serum sickness. Further work showed that antigen-antibody complexes were visible in the lesions as they developed. This was strong evidence that the antigen-antibody complexes themselves worked like a pathogen, not just sign-posting disease, but actually causing damage to the tissue. Dixon's work at Pitt showed how our antibody response, which was thought to keep us healthy, could actually make us sick.

A new field, immunopathology, arose to describe what happens when our bodies' own defenses turn on us. Dixon assembled a group of young researchers high atop the hill in Pennsylvania Hall, where, since it had been left by the rest of the medical school for the new Scaife building, he had unlimited space. Clinical duties were carried out by an arm of the department dedicated to that task, so his crew spent a lot of time in their labs. With Dixon's radioactive iodine tracers and another new technique for making proteins glow under ultraviolet light (immunofluorescence), they had the quantitative and visual tools to start answering the flurry of questions raised by Dixon's early serum sickness work: How many antigens does it take to cause disease? How long must they circulate in the blood to be harmful? Do all

antigen-antibody complexes cause disease? Why do they land in the kidneys?

"You didn't have to be a rocket scientist to think of a problem," Dixon says. "They were all there." He was likely to pose physical challenges to his faculty, too. Because he didn't like to sit for long, he was often encouraging the others to join him in a lunchtime run or a game of squash.

Dixon's energetic group was the first to realize that the immune response can result in two types of kidney disease. In one, the antigen-antibody complexes get stuck in the glomeruli of the kidney and attract disease-fighting white blood cells that cause inflammation, as in lupus; in another, antibodies attack the kidney directly, as in antiglomerular basement membrane (anti-GBM) disease.

Also among their firsts: They figured out how to transfer anti-GBM disease antibodies from a human to a monkey, which made the monkey sick and definitively proved that the antibodies were the cause.

Each week, Dixon gathered the faculty and fellows together to discuss their work. Sometimes they grilled each other ruthlessly. If a scientific meeting was coming up, they practiced their talks. Even if the topic in question wasn't his area, Dixon always had a cogent question that cut to the heart of a subject, revealing where more detail was needed. When the phrase "Don't you think?" rang out in Dixon's clear voice, they knew he was about to home in. These rigors prepared his faculty not only for presenting at scientific meetings but also for running their own organizations: A half-dozen of Dixon's fellows from Pitt went on to become department heads elsewhere—at the University of Colorado, at Washington University, and at what's now the Medical College of Pennsylvania-Hahnemann, to name a few.

**When the phrase "Don't you think?" rang out in Dixon's clear voice, they knew he was about to home in.**

Immunopathology was so new it spawned just one or two national meetings each year, and everyone seemed to know everyone else in attendance. During the meetings of the Federation of American Societies for Experimental Biology, a lot of science was discussed on the Atlantic City boardwalk or in the hotel bar. Such association meetings were as social as they were scientific, and much of the fraternizing revolved around Dixon, who could revel as intensely as he worked. The stories he told could make a longshoreman blush. He was likely to get on a table and lead a Marine corps charge. At a meeting in Switzerland, where it is customary to leave one's shoes in the hotel hallway overnight to be cleaned, he secretly moved the second-floor guests' shoes to the third floor and the third-floor guests' shoes to the second floor.

Still, he didn't stay away from the lab for as long as planned, not even on family trips. Each summer the Dixons would get away, usually to Cape Cod, Massachusetts, where he and his wife, Marion, would go for long ocean swims, often as far as a mile. (They once returned to the house itching from small critters in their suits. Dixon took a few down to the lab at Woods Hole for analysis: They were baby lobsters.) Though the Dixons usually planned to be away for a set month, they always seemed to come home to Pittsburgh a day or two early. That was the only sign Dixon showed of the weight of running a department. He never came home from work beleaguered; instead he was likely to reenergize himself with his oft-repeated maxim, "When the going gets tough, the tough get going."

By 1960, Dixon's work in Pittsburgh had come to the attention of Edmund Keeney, the allergist running the Scripps Clinic in, of all places, La Jolla, California, who wanted to start a research program. Scripps was unknown then; it was just a small-town hospital with an allergy clinic. This was a risky career move. But La Jolla offered Dixon the possibility of fulfilling his professional and teenage dreams: There would be no teaching duties, no medical school administering, just pure, autonomous research, along with miles of beach and endless summer. He and Marion chose a sprawling stucco house with ocean views and decorated it in cool gray tones. During long walks on the beach with their dad, Dixon's three children collected pebbles; he polished the rocks in a tumbler in the garage, then gave them a special place in the living room.

As the chair of the Department of Experimental Pathology for the Scripps Clinic and Research Foundation, Dixon lured six postdocs, a half-dozen support staff, and four faculty members with him from Pitt to La Jolla, where many remained for the rest of their careers. Scripps had only space and good will; Dixon and his team needed grants to cover their salaries and operating expenses. Fortunately, Dixon already knew the formula: Spend lots of time in the lab, do great science, write good papers, give the best talks, submit sound proposals, get the money . . . . He'd already taught it to the faculty he brought with him from Pitt, and everyone he recruited thereafter was expected to do the same. While at Scripps, Dixon attended scores of scientific meetings to get out the word about the institute and his faculty's research. One year he spent 200 days away from home. As the institute grew, he became chair of the biomedical research departments, then director of the Research Institute of Scripps Clinic.

He was, nevertheless, in the lab as much as possible. Dixon further elucidated the kidney diseases he had discovered at Pitt. Another project, a collaboration with Thomas Starzl, showed the world that a transplanted kidney can fall prey to the same antibody-inflicted disease that damaged the patient's original kidneys, even if the new kidney came from an identical twin. Later, in a few otherwise understudied mouse strains that spontaneously develop lupus, he found an ideal animal model for exploring the immunopathology of the disease. His associates at Scripps are now close to describing the cause of lupus, which looks to be a series of genes that are benign in isolation but, when inherited as a suite and triggered by environmental factors, make the immune system attack the body's DNA.

Dixon stepped down as director in 1986, though he continued his research for several more years. Now he enjoys having no vocation. Friends work with him on his bonsai garden. He and Marion walk the poodles on the beach. He has just stepped down from editing *Advances in Immunology,* which he'd overseen for 35 years. Still, talking science animates him. He'll punctuate sentences with "Okay?" or "Right?" to make sure he is understood. When asked if, in building institutions, he followed the tenets of any particular management school, he scoffs.

"I have no idea what you're talking about," he says.

"You work like hell. First of all you raise the money, and then you work like hell, and everything works out." ■

WITH OLIVERA FINN, IMMUNOLOGY MAKES A BIG SPLASH AT PITT | BY DAVID R. ELTZ

# THE DIRECTOR

Drama was Olivera Finn's first love. Growing up in Nis, then an industrial Yugoslavian city of 100,000, she longed to become a theatre director. Often a teacher would gather together her class and pack everyone off to the national theatre for the afternoon. "Olja" (pronounced "Olya") would sit riveted before the stage as the actors played out Yugoslavian and Shakespearean drama, planning how she would someday run those same plays.

Her father had different ideas. A journalist and novelist who'd published theatre criticism, Dragi Jankovic, saw English and science as the wave of the future. As a first step toward preparing his girl, he enrolled her in an English class two nights a week at the local workers' university. She was in first grade. Her lessons lasted eight years. When it came time to choose a high school, Finn could attend either the arts and language school or the math and sciences school. Jankovic cut a deal: His daughter could pursue the theatre only if she graduated from the math and sciences school.

It was a nifty trick. But Jankovic's plan for his daughter's future took a detour. At 16, his English-speaking girl met Seth Finn, an American student from Brown University visiting Nis on a summer study program. Two years later, after he completed a Fulbright Fellowship and she finished high school, they were married and off to the States. Today, in a way, the Stanford-trained PhD is directing her own play. In October, Olivera Finn was appointed acting chair of the School of Medicine's new Department of Immunology.

She has a couple of hard acts to follow. Nobel prize laureate Niels Jerne, a leading theorist on the primary immune response whom some considered the "conscience" of immunology, was chair of microbiology at Pitt in the '60s. Frank Dixon, chair of the Department of Pathology in the '50s, became one of the first immunopathologists. Finn is eager to build on this legacy.

At Stanford University in the early '80s she worked on then-developing research on the role of proteins that help activate T cells to fight cancer. At Duke University Finn set up a tumor immunology lab, where she discovered a tumor protein that T cells recognize as foreign. She created a synthetic version of the protein, and used animal studies and clinical trials to show how it can elicit an immune response to kill tumor cells upon first glance. She had, in effect, made a vaccine for such carcinomas as pancreatic and breast cancer, which she has patented and continued to test since moving to Pitt in 1991. (Her work continues to bear fruit—see the cover story in November's *Journal of Experimental Medicine*.)

Finn says it has been necessary for her to try to change "the culture" through the years of those at the National Institutes of Health and Food and Drug Administration who hesitate to allow the vaccine to be used for cancer prevention. Her critics fear the vaccine will somehow trigger an attack on normal tissue. She has also encountered more than her share of people who say, "I agree with you," but still won't allow her to proceed beyond Phase I trials. "That still doesn't mean you shouldn't fight for what you think should be done," she says.



Finn has developed a cancer vaccine, now she's ready to develop a program that uncloaks the immune system.

CRAIG THOMPSON; LA PRIMA CAFE, PITTSBURGH

More than her own interests, Finn views her newly anointed mission much like Jerne and Dixon did theirs; she is interested in pulling the cloak off the basic workings of the immune system. "I want to have people doing the newest immunology areas—immunogenomics, immunoproteomics, signaling—people who do immunology just to discover how things work," she says passionately. "We have great people here who try to understand how the immune system works in cancer, transplantation, and autoimmunity. We need to bring people here who do immunology just for the hell of it."

**"I perhaps do not know anybody else who has the extraordinary ability to say the truth plainly, to say even the most unpleasant truth plainly, without offending anyone."**

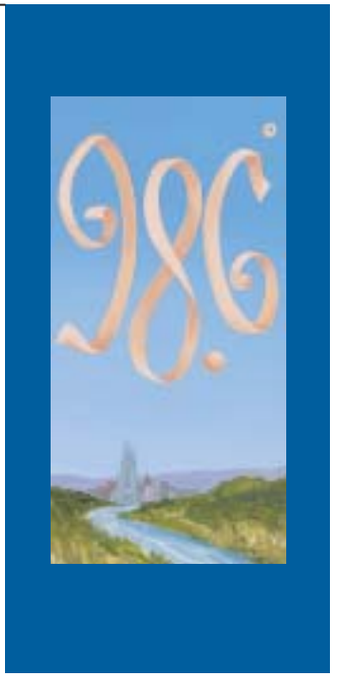
One has the sense that Finn is more than up to the task of recruiting Pitt's next generation of immunology stars. At meetings with the cancer establishment she has convinced people at least to listen to her—no small triumph, as one colleague notes. Another colleague, Pramod Srivastava, director of the Center for Immunotherapy of Cancer and Infectious Diseases at the University of Connecticut, says, "I perhaps do not know anybody else who has the extraordinary ability to say the truth plainly, to say even the most unpleasant truth plainly, without offending anyone. It is a rare trait and invaluable for someone trying to build a department."

Perhaps it helps that Finn, a lover of things theatric, has a flair for the moment. During her first year as a faculty member at Duke, the department chair sent her an invitation to a picnic. It was addressed to "Dr. and Mrs. Seth Finn." When she complained, the chair brushed it off—"You just don't know the protocol." Finn remarked, "That protocol needs to die a quick death."

She later discovered that in the department secretary's desk was a list of doctors' names, all male; wives were listed alongside in parentheses (as was Finn). Her husband was listed as the department member. Funny thing was, Seth Finn, though also a PhD, was a communications professor at the University of North Carolina at Chapel Hill. At the next faculty meeting, Finn's motion to change the protocol passed. Afterward, the chair approached her. "Okay. What do you want me to call you?"

Finn smiled, saying, "I'm sure my paycheck doesn't say 'Mrs. Seth Finn.'" ■

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




# UNANSWERED KILLER

## MILLIONS GO TOWARD UNDERSTANDING IPF

BY DAVID R. ELTZ

The only picture on the desk of Dick Simmons, the retired chair of Allegheny Technologies who once marshaled a gutsy $195 million buyout of a steel manufacturer during the industry's darker days, shows him with his wife of 42 years, Dorothy, and two grandchildren. No clouds muddle the turquoise sky in the background. It is an image of a pleasant vacation, a simple moment last January in Boca Grande, Florida, for a family in which, says Simmons, "the men go out into the world and do battle, and the women stay home and do their own battle."

It is difficult to guess that the photograph was taken weeks before Dorothy Simmons would lose her toughest battle—with an incurable disease—because to look at the picture is to gaze upon a family seemingly in control of life. One recent day as Simmons looks above the photograph, out the window of his Pittsburgh office, tears welling up in his eyes, that false impression fades as quickly as the fragile veil of good health sometimes does.

Dorothy Simmons was diagnosed in 1995 with idiopathic pulmonary fibrosis (IPF), a degenerative lung disease in which the interstitium, the air sacs of the lung, become scarred and unable to process oxygen. For the next six years she and her husband hunted for answers. What is the cause? What are the effective treatments? Inevitably the question became, How much time is left?

"We don't know," the doctors would say, again and again, in a refrain familiar to the estimated four to 10 people in every 100,000 who get this disease. The questions outnumbered the answers, and shortly before Dorothy Simmons died the couple pledged a total of $5 million to the University of Pittsburgh. The gift created the Dorothy P. and Richard P. Simmons Center for Research and Education in Interstitial Lung Disease and an endowed chair for pulmonary research.

Typically IPF affects the elderly, but it is not unheard of for someone to be diagnosed in his or her 30s. It was once thought IPF's cause could be related to environmental and occupational conditions that perhaps trigger the disease. That might be so, and it might not be. "We don't think there's a clear relationship," says Kevin Gibson, an associate professor of medicine investigating the disease. "You'll see IPF all over the country, in areas where there's no industry."

Often people will develop a cough prior to diagnosis. Sometimes they're misdiagnosed with pneumonia, tuberculosis, or chronic obstructive pulmonary disease. Among those diagnosed correctly, usually following an open lung biopsy, some lose ground gradually, others quickly. Some become sick and get better, then become sick and get better again. The sickest patients are told they have four to seven years to live. The only known cure is lung transplantation.

Treatments vary. Many people with IPF need a constant influx of tanked oxygen. Most receive steroids, because doctors have thought of the disease as an inflammation of lung tissue. Today, though, Gibson says, doctors typically believe the number of people who will benefit from steroids is something like 15 of every 100 people who take them. Gibson, also the associate director of the Simmons center, is part of a team conducting a Phase III trial of interferon gamma, a drug originally developed to treat cancer that might show some promise in thwarting IPF.



COURTESY SIMMONS

**Dorothy Simmons with one of her grandchildren in 1996.**

The center makes great effort to let patients know what doctors do know. It is establishing a comprehensive website (http://www.ipf.upmc.com) and a patient support group. The group meets bimonthly, bringing patients together with doctors and other health care professionals for a few hours in a comfortable atmosphere to discuss the disease.

"You can see other people with the disease," says one support group member in his 40s. The meetings give the man, diagnosed with IPF two years ago and now on oxygen full-time, a chance to measure himself on the scale of IPF's severity. And he can talk to doctors. "You can see the very bare honesty, that they don't know—and that's a hard pill to swallow—but you can talk one on one with them. You're more than just an appointment." ■

**FOR MORE INFORMATION: 412-802-3274**



PHOTODISC

The FAST mentoring program helps students make their way.

# WE BELIEVE

## A SUPPORT NETWORK—DELIVERED FAST

BY DOTTIE HORN

Reading EKGs, distinguishing a systolic murmur from a diastolic murmur—not exactly a piece of cake. Every med student is bound to have one class that seems to take a lot more effort than the rest. For Alison DeLuca, MD '04, it was second-year cardiology. *I could take a year off,* she began to think. *Maybe get a master's degree in public health or ethics.*

Then she got a call from her adviser, Margaret Ragni, MD '75, professor of medicine at the University of Pittsburgh. The two had met several times the previous year as part of the Faculty and Students Together (FAST) mentoring program. Every incoming first-year student becomes part of a FAST group consisting of one faculty adviser, four first-year students, and two second-year students who serve as "big sibs." FAST groups meet occasionally throughout the student's four years of school. They might gather at their adviser's home for dinner, carve pumpkins together, or maybe go to a concert to unwind. For several years at Pitt, FAST has given students an instant support network and, often, a needed recharge, notes Joan Harvey, the associate dean who runs the program.

Ragni's call came at the beginning of DeLuca's second year, when the professor was touching base with her FAST mentees. They made plans to have lunch in the hospital cafeteria. When they met, DeLuca told Ragni that she was thinking of getting a master's. But the prof soon discovered that DeLuca wasn't so drawn to a degree in public health and ethics as she was ready for a change of pace. Ragni learned her mentee was eager to be in a clinical setting, seeing patients.

*Wait until third year,* she told the 23-year-old DeLuca. *Third year's going to be great.* That reignited the student's excitement about her future and helped her feel less overwhelmed. They got to talking about DeLuca's interests in art, literature, and writing.

*You should read Therese Southgate,* said Ragni. DeLuca already did. The two discovered they are both fans of Southgate, a physician who writes a weekly commentary about the art featured on every cover of the *Journal of the American Medical Association.*

DeLuca revealed that she liked to imagine herself becoming the next Southgate.

*You can make your career what you want it to be,* Ragni said. *We'll find a way to make it work.*

Such advice is typical of the encouragement that Ragni gives her FAST mentees. "They just need to believe in themselves," she says. She'll share stories from her own life to demonstrate. In her animated voice, she might tell them what happened one Sunday in 1985, when she was a spokesperson for the Pittsburgh blood bank. A television station wanted an interview, and she was at home with her two children, a 4-year-old and an 18-month-old. Since her husband was at work, she packed the children in the car and headed to the blood bank. But her youngest daughter wouldn't let go of her leg during the interview. The camera crew accommodated, shooting Ragni from the waist up and cropping her clinging child out of the picture.

"The students love to hear stories about how you make it work," she says.

"The fact that I did what I wanted to do empowers them. They think, 'Hey, why can't I also?'"

Ragni's example has not been lost on DeLuca. She is confident that she will find her niche. "It's exciting to know there are so many possibilities," DeLuca says.

And the possibilities keep presenting themselves. DeLuca has been interested in psychiatry for a while; she just discovered a "huge link" between endocrinology and psychiatry.

"That's my new thing," she says, with a passion not so unusual for a student unraveling the wonders of the human body.

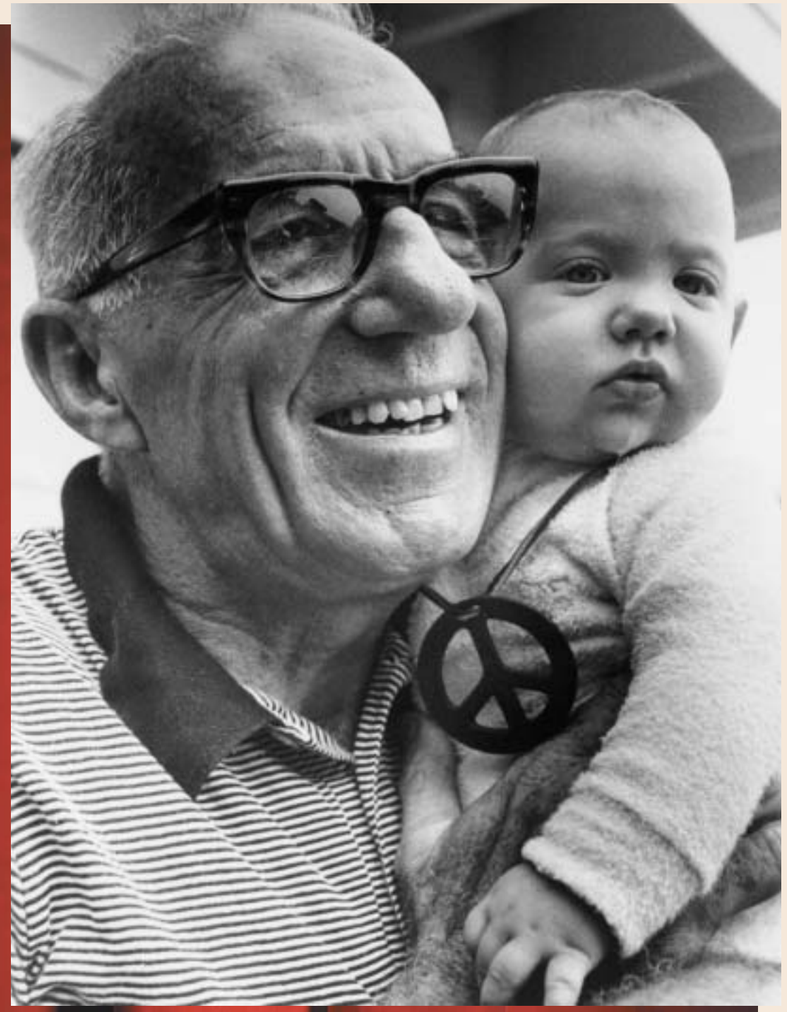
"I've got to let Dr. Ragni know I'm so excited about endocrinology and psychiatry." ■

### LEAN ON ME

**If you enroll in med school at the University of Pittsburgh, your family circle widens. Immediately. As part of the Faculty and Students Together program, med students are adopted in their first month at Pitt by two "big sibs," more senior students who make sure newbies don't think they have to go it alone. Alison DeLuca, MD '04, especially appreciated her new sibs during her first year. After a big exam, they would leave treats in her mailbox—homemade chocolate chip cookies, candy, congratulatory notes. And they doled out lots of wisdom and encouragement: *Here's what to concentrate on for the exam. Don't get stressed. Everyone's in the same boat. Dr. Schumann is the best!* "It's not so much the academic advice that really matters as the support," says DeLuca. *—EL & DH***

# SPOCK'S BABY

**THE FAMOUS DOC NURTURED PITTSBURGH CHILDREN | BY EDWIN KEISTER JR.**



The Arsenal Family and Children's Center, established by Benjamin Spock, is one mark he left on Pittsburgh. The avuncular yet rebellious doc served as a faculty member at Pitt in the '50s. (Above photo, 1969)

His *Baby and Child Care* sold more than 50 million copies; his soothing words on feeding schedules and toilet training reassured a whole generation of nervous baby-boom parents; his name became a revered household word. Later, Benjamin Spock demonstrated against the Vietnam war, was jailed and convicted of "conspiracy to aid, abet, and counsel young men to avoid the draft" after a march at the Pentagon (the conviction was overturned), and quixotically as well as unsuccessfully ran for president and then vice-president. But one chapter in the celebrity doctor's career is often overlooked: his five formative years as a faculty member at Pitt and the important imprint he left behind. Indeed Spock himself, in his memoir *Spock on Spock,* never so much as mentions Pittsburgh.

But at the Arsenal Family and Children's Center in Pittsburgh's Lawrenceville district, the Spock legacy is by no means forgotten. He founded the center with child-development specialist Margaret McFarland.

"Dr. Spock founded our center to focus on healthy child development," declares Von Kearins, Arsenal's current director who now occupies the large mahogany desk that Spock brought to the center in 1951. "And we continue to carry out his focus."

Spock came to Pitt from the Mayo Clinic with his reputation already established. Duell, Sloan, and Pierce published his *Baby and Child Care* in 1945 after Spock served two years in the navy. Pocket Books' paperback edition—Spock insisted it be sold at 25 cents—was quickly found at virtually every crib side in the country. The author, a child psychiatrist by training, provided avuncular advice on almost every parental worry, free of medical jargon. Rather than adhere to the old, rigid, child-rearing rules, he told parents to follow their instincts and foster the child's emotional growth. Says Jonathon Erlen, a medical historian at Pitt, "His message to parents was, 'Trust yourself.'"

BETTMAN/UPI

"Pittsburgh has taken a long stride toward its goal of becoming one of the world's leading medical centers," exulted the *Pittsburgh Post-Gazette* in November 1950, greeting the simultaneous appointment to the Department of Psychiatry of Spock, Henry Brosin, and Arthur Mirsky. The article identified the new appointees as "three of the nation's top psychiatric experts."

Spock established a child development clinic at Western Psychiatric Institute and Clinic. It's mission was to conduct research in children's healthy development and serve as a training ground for pediatricians and psychiatrists.

The Arsenal center, a couple of miles away, was one of Spock's first projects in Pittsburgh. "He believed that the emotional well-being of children was at least as important as their physical health," says Keairns, who came to the center in 1968. "His attitude was that we should not wait for emotional problems and then treat them, but develop an atmosphere in which they did not occur in the first place. And the way to do that was to work with families and strengthen the family environment via a friendly neighborhood center. He chose Lawrenceville because its high-ethnic, less-mobile population seemed to guarantee continuity for the program."

**"His attitude was that we should not wait for emotional problems and then treat them, but develop an atmosphere in which they did not occur in the first place."**

He recruited Erik Erikson, the great guru of child development, to lecture monthly to pediatric and psychiatric residents. Fledgling physicians should understand normal child development as well as treat illness, Spock maintained. A similar program continued well after Spock and Erikson left, until Pitt severed its ties with Arsenal in 1979 after a series of funding crises. Private funding now supports "Spock's baby," which now trains Duquesne University psychology students. But it still follows its founders' vision from 50 years ago.

Spock and McFarland were right; the Lawrenceville community proved cohesive, which made tracking children easier. "We have Italian, Irish, Slavic families who have been coming here through three generations," she says. Parents and children come together to the center, where parents are taught to observe and understand their children's behavior. "We see many kinds of families Dr. Spock might not have envisioned," Keairns says. In its special programs, Arsenal works with parents who have been estranged from their children for various reasons, including drug abuse. "But our point of departure always is—what are the children telling us they need?" says Keairns.

For example, Arsenal continues to carry out Spock and Erikson's idea that play is a child's most important learning tool. Arsenal's "play curriculum" tells staff and parents to watch closely children's play interests and then to furnish materials to enhance those interests. "We had a 3-year-old who was interested in dinosaurs," Keairns says. "Not just a child's ordinary fascination with dinosaurs. Real, deep, abiding interest, going beyond dinosaur toys. We furnished picture books, field trips to the Carnegie Museum's dinosaur collection, et cetera." She pauses for emphasis. "He is now an associate professor of geology at Southwest Texas State University specializing in paleontology."

In 1953, with booming book sales and a monthly column in *Ladies' Home Journal*, the Pitt professor became a television personality, too. His live, half-hour weekly program aired on public TV and then on NBC.

Spock's eventual departure from Pitt can probably be summed up as classic academic infighting. According to his biographers, colleagues complained that Spock published popular books and magazine articles but had produced only two scientific articles in his Pitt career; others postulate that he concentrated too much on child development and not enough on existing psychiatric problems.

He saw himself as a lax administrator. "It was a job calling on some skills which I found that I didn't have," he told biographer Thomas Maier years later.

His department chair, Henry Brosin, was strong-willed. The two quickly clashed, especially about Spock's right to choose his own clinical staff. Several times throughout 1954 and 1955, Spock submitted his resignation over the issue. Robert Moore, vice-chancellor for medical affairs, persuaded Spock to stay but yield his administrative duties. Brosin personally took over the clinic at Western Psychiatric. Mirsky, among the three recruits the *Post-Gazette* had dubbed "the finest psychiatric team in America," later said, "Ben could have had anything, but because he was so convinced by Brosin that he was a lousy administrator, his productivity and career were permanently impaired." In June 1955, Spock submitted his resignation again; this time it was accepted.

After Pitt, Spock became increasingly enmeshed in national issues, especially the antinuclear and antiwar movements. In the turbulent '60s, politicians and other critics blamed his book for a generation raised on permissiveness that was disrespectful of authority. (Spock denied favoring permissiveness, but in later editions of his book he called for more parental firmness.) Decades later, even his progressive tendencies echo in Pittsburgh. On behalf of the Quaker office at the United Nations, Keairns is researching how young female child soldiers in Africa, Asia, and South America can reintegrate themselves into family and community life.

"I like to think that role is more evidence of Dr. Spock's influence," she says. ■



# CLASS NOTES

## '50s

**Ralph J. Miller Sr.**, MD '52, a urologist with a private practice in Indiana, Pennsylvania, has been doing some writing. He recently published *Doctor in Jeopardy* (Aesculapius Publishing). The book, which details his experiences in medical school and as a local community hospital doctor struggling to improve health care, is available at the University Book Center and at http://www.atlasbooks.com. His son, Ralph Miller Jr., MD '84, also is a urologist.

## '60s

**Thomas J. Martin**, MD '60, has spent the past five years as team physician for the football program at Pennsylvania State University after serving as chair of pediatrics at Geisinger Medical Center and the Janet Weis Children's Hospital in Danville, Pennsylvania. Even though he tapes up a sworn rival team, Martin confesses he's still a Panther fan at heart.

**Harvey Rosenbaum**, MD '61, joined the Cleveland Clinic in 1997 after 29 years of private practice in internal medicine and endocrinology. Rosenbaum trained at the clinic, and the recent opportunity let him return to those familiar surroundings. At his 40th reunion, he was pleased to learn that women make up half the students enrolled at Pitt med today; only four out of 100 students in his class were women. He notes that Pittsburgh has changed, too—in 1957, his wife used to clean the window sills twice a day.

**Maurice Mahoney**, MD '62, a Yale University School of Medicine professor, has played an integral role in the school's Institutional Review Board since 1987. Last year he was named executive director. Says Mahoney: "I've always had an interest in human subject protection in clinical research and in the ways we conduct it." It's also a perfect way for him to apply his recently acquired law degree.

**Edwin Morgan**, MD '64, retired last year as director of the University Health Service at West Virginia University in Morgantown. Morgan recalls how Gene Robin, professor of medicine at Pitt, encouraged his interest in pulmonary diseases. As a medical student on rotation at Mercy Hospital, he met his future wife, Naomi. At Mercy, he also worked with Rick Siker, who helped him secure an elective in Cardiff, Wales, where he later did a fellowship in occupational lung disease.



**"Miss Pitt,"** ***The Owl*****, 1953**

## '70s

**Russell J. Sacco**, MD '71, is an internal and geriatric medical specialist at UPMC Shadyside. In May, he was elected a fellow of the American College of Physicians-American Society of Internal Medicine. His son, David Sacco, received his MD from Pitt in 2000.

**Daniel Hankins**, MD '74, the co-medical director of Mayo Medical Transport and the Emergency Communications Center at the Mayo Clinic, has been researching the effectiveness of automated external defibrillators and helicopter transports in emergency situations. His research shows that both increase patients' survival rates. Governor Jesse Ventura recently appointed Hankins chair of Minnesota's EMS Regulatory Board, in which capacity he will oversee and craft policy for paramedics statewide.

**Johanna Seddon**, MD '74, an associate professor of epidemiology and ophthalmology at Harvard University, published an article in the October issue of *Archives of Ophthalmology*. Her research concludes that elderly patients who take vitaminas C and E, beta-carotene, and zinc reduce their chances of contracting advanced macular degeneration. Seddon directs the epidemiology unit at Massachusetts Eye and Ear Infirmary.

**Jackson T. Wright Jr.**, MD '76, PhD '77, is a professor of medicine at Case Western Reserve University. He is vice-chair of the steering committee and a PI

## DIXIE DOC | RICHARD PAUL SPEAKS IN NOTES

EDWARD J. HUMES

On a bike tour two summers ago, Richard Paul, MD '61, coasted into a small town in France. It was market day, and a street band was performing. The other bikers stopped to listen, but Paul grabbed the cornet he takes everywhere he travels. Still wearing his helmet, he jumped in, picking up the tune with ease.

Paul, a retired Pittsburgh pediatrician, didn't need to speak French. He and the street band shared the only language they needed: music. It has always been that way for Paul, the leader back home of a dixieland band.

"Medicine is a very difficult gig," he says, "It can't be all consuming." Doctors need diversions, Paul says, and music always has been his. One fall evening, Dixie Doc and the Pittsburgh Dixieland All Stars play at Penn Brewery, in the heart of Pittsburgh's Germantown. Paul sits in front of the group, resting his horn in his lap. Then he stands, putting trumpet to lips and rousing the crowd to applause. When his solo is through, he sits, smiling, tapping his foot, waiting for the next cue to come around.



"Mr. Pitt,"
*The Owl*, 1953

for the multicenter African-American Study of Kidney Disease and Hypertension. With his study colleagues, he recently published an article in the *Journal of the American Medical Association* showing that Ramipril slows the progression of hypertensive renal disease and proteinuria.

## '70s RESIDENTS AND FELLOWS

**Michael Landay**, MD '68 (Internal Medicine Resident '70), was recently appointed Jack Reynolds, MD, Chair in Radiology at the University of Texas Southwestern Medical Center in Dallas. Landay became interested in radiology during a tour of duty in Vietnam, where he was inspired by a colleague's example.

**Carl Fischer** (Pediatric Anesthesia Fellow '72), completed research at the Shriners Burns Hospital in Cincinnati, Ohio, showing that using local anesthesia can make skin grafts for burn patients less painful. (If a local anesthetic is incorporated in the Pitkin solution at the donor site, a much less systemic narcotic is needed to make the patient comfortable—especially in the first 24-36 postoperative hours, Fischer says.)

**James Peoples** (Surgical Intern '72, Surgical Resident '77, Surgical Teaching Fellow '77), chair of the Department of Surgery at Wright State University in Dayton, Ohio, organizes a wine auction each year that raises about $25,000 a year for the regional chapter of Planned Parenthood. He notes: "I work at Planned Parenthood as a fund-raiser not because I'm a doctor but because it's a good organization."

## '80s

**Carol Slomski**, MD '81, recently was appointed associate dean for graduate medical education at Michigan State University's College of Human Medicine. She's also community assistant dean for the Lansing campus.

## '80s RESIDENTS AND FELLOWS

**Vincent Verdile** (Emergency Medicine Intern '85, Emergency Medicine Resident '87) was recently appointed dean of the Albany Medical College in Albany, New York. Verdile says he loves the administrative aspect of being dean because it reminds him of his younger days. Overseeing the activities of department chairs, professors, and students in some ways reminds him of days spent managing the needs of chefs, prep cooks, and customers at his family's Italian restaurant. By the way, if you're ever in Troy, New York, go to Verdile's.

## '90s

**Robert W. Neumar**, MD '90, assistant professor of emergency medicine at the University of Pennsylvania, is investigating the cause behind brain cell death following ischemia in order to improve current therapeutic methods. His recent study about activation of protease cascades after injury appears in the July issue of *Experimental Neurology.*

**Keith Williams**, MD '95, clinical instructor of internal medicine for Boston University, works with the Boston Health Care for the Homeless Program. He also sees clients from an alcohol and drug detoxification program called Bridge to Recovery. —*MH*

## THE WAY WE ARE: CLASS OF '76

BY EDWARD J. HUMES



Sally G. Osborne, MD '76, remembers July 4, 1976, well. She was on rounds at Magee-Womens Hospital; it was her first birthday as a doctor. As she settled into a night's work, she looked up at a television to see revelers gathering on the streets of New York to celebrate 200 years of American independence. Like everyone from the Class of '76, she was just beginning her career. The holiday would have to go on without her.

By 1999, a series of neck injuries limited sensation in Osborne's right arm, ruining her ability to perform surgery. Osborne, an ob/gyn, became director of a Tampa Bay, Florida, research group that examines women's



Richard Paul, on left, pulls out his horn as the mood hits.


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Members of the Class of '76 gathered in Pittsburgh in October for their 25th reunion.

health issues. She also sits on the Florida Medical Association's Council on Ethical and Judicial Affairs.

On the nation's bicentennial Pitt also begot Alvah R. Cass, MD '76, now of the University of Texas Medical Branch at Galveston, who directs that university's research in family medicine. He received a master's in epidemiology from Harvard University in 1996. Cass examines bone density studies, to develop better standards for early detection of osteoporosis in women and men. His Pitt classmate, Rodney Hornbake, MD '76, is senior vice-president of Gentiva Health Services. The company provides services to patients with rare chronic disorders like hemophilia and pulmonary hypertension; it also supports clinical trials. At Hofstra University, Hornbake teaches in a graduate program for physician leaders and health care managers.

Osborne joined some 30 members of the Class of '76 at Pitt in October. Thanks to the hard work of University of Pennsylvania radiologist and reunion organizer Margaret LaManna, MD '76, they celebrated their reunion in style at the Grand Concourse. The group missed the Homecoming fireworks. But unlike that residency shift 25 years ago, this time Osborne got to sit back and enjoy the festivities.



LIVE FROM BEANTOWN: Pitt took Dean Arthur S. Levine, Alan Russell, director of the McGowan Institute for Regenerative Medicine, and Alan Meisel, director of the Center for Bioethics and Health Law, on the road to Boston in October to discuss the potential of stem cell research before about 170 University of Pittsburgh alumni. More Pitt Med: On the Road events are planned for Florida, Washington, DC, and California.

## WE KNEW YOU WHEN, CAMPBELL MOSES



Moses, 1941

For a decade, Campbell Moses (MD '41) hosted *Grand Rounds,* a medical-education television program in Pittsburgh aimed at doctors. "It was promoted in the local newspapers: 'Don't call your doctor between noon and 1 p.m. on Friday; he'll be taking a postgraduate course,'" Moses remembered during the recent Homecoming weekend.

His career began in 1942 at Pitt as an instructor of physiology and pharmacology. By 1957, Moses had helped the School of Medicine obtain grants to start the Addison H. Gibson Laboratory, a research facility he directed (marking Pitt's return to live animal studies), and the University's first radioactive isotope program. He would go on, in 1967, to head the American Heart Association for a decade, before retiring in the '80s from a New York medical advertising agency that produced interactive educational videos for hospitals. Today, now mostly retired, Moses divides his time between his homes in Manhattan and Spring Lake, New Jersey. *–DRE*



Moses (seated, left) at his reunion in October with former classmates. Standing from left: Richard Harrison Bulger, Raymond Frederic Grenfell, James Thomas McLaughlin, Sidney Stanley Kaufman. Sitting with Moses: James Stanton Tipping, Betty H. Bradley, William Karl Sieber.

## IN MEMORIAM

### '20s

**L. HARVEY STEELE (MD '29)**
AUGUST 6, 2001

### '30s

**CYRUS P. MARKLE JR. (MD '37)**
SEPTEMBER 26, 2001

**ANGELO A. PETRAGLIA (MD '38)**
OCTOBER 21, 2001

### '40s

**EMMA WEBB CLARKE (MD '47)**
JANUARY 31, 2001

**ROBERT H. CLARKE (MD '47)**
AUGUST 19, 2001

**GEORGE C. WRIGHT JR. (MD '49)**
OCTOBER 11, 2001

### '50s

**M. DOROTHY BURNS (MD '53)**
FEBRUARY 8, 2001

**EDWARD R. SEITZ (MD '54)**
SEPTEMBER 16, 2001

### '60s

**JAMES M. POMARICO (MD '63)**
AUGUST 15, 2001

**WILLIAM E. BROWN (MD '64)**
OCTOBER 12, 2001

**DONALD S. FRALEY JR. (MD '68)**
NOVEMBER 14, 2001

# TIMOTHY EBERLEIN: IN THE RIGHT PLACE

BY MEGHAN HOLOHAN



As a resident, Eberlein thought for a moment that Harvard was about to fire him; instead the school extended him an offer.

When Kim Johnson walked into an undergraduate biology lab in 1972 at the University of Pittsburgh, Timothy Eberlein leaned toward his lab partner and boasted that she would be his future wife. His partner laughed, doubtful, but Eberlein knew.

After a few dates, Johnson wasn't sure about Eberlein. She thought he was too serious; she wanted a career. But he knew they would marry. Two and a half years later, they did.

Eberlein, MD '77, says he is one of those people who sometimes happens to be in the right place at the right time. He credits meeting his wife to "divine intervention," and he believes a chance to witness an aortic surgery at the Veterans Affairs hospital in Oakland led to his career in surgery. Eberlein does this a lot, attributing his accomplishments to happenstance. His actions tell a different story.

As chair of surgery at Washington University in St. Louis, where he specializes in treating breast cancer, he brought National Cancer Institute (NCI) recognition and funding to the Alvin J. Siteman Cancer Center just three years after his arrival. "That's obviously a tremendous reward for a lot of hard work by a lot of individuals," he says. Eberlein himself is notorious for putting in 18 to 20 hour workdays.

It's not surprising that, decades earlier, as a second-year resident at Brigham and Women's Hospital, he one day received a page from the chairs of surgery and oncology at Harvard University. They wanted to see him immediately. Thinking he was getting fired and wondering what he did wrong, Eberlein trudged off to meet them. When he arrived, they told him they didn't want him to leave the institution. *Would he like to join the faculty?* He accepted the offer, and 10 years later became chief of Harvard's division of surgical oncology.

And he doesn't give up easily. When he trained at the NCI in the early '80s, Eberlein began researching the protein IL-2, high concentrations of which, he theorized, might elicit immune systems to eradicate tumors. Eight years went into the investigation, only to find out "it just doesn't work" as an immune-response cure as he thought it might. (Though IL-2 *is* used as a treatment for advanced melanoma and kidney cancer.)

Today he believes he has developed a cancer vaccine, currently in a Phase I trial. It's a peptide called GP2, derived from the HER2/nue gene. In ovarian, breast, pancreatic, and other cancers, the HER2/nue gene propagates out of control. Eberlein thinks GP2 could help people's immune systems resist these cancers. "Our hope is not to cure cancer in a Phase I trial," he says, "but to understand how this immune response works, and how we can make it better."

**He brought NCI recognition and funding to the Alvin J. Siteman Cancer Center just three years after his arrival.**

Eberlein's colleagues speak of him as a talented surgeon, researcher, and department chair known for his willingness to burn the midnight oil. But his family notes his energy carries into all aspects of his life. Eberlein's passions include golf and hockey, a sport he watched his son play for many years. Mentoring has become a passion of his as well. Eberlein enjoys fostering the careers of those around him as well as faculty at other institutions. It's not unusual for him to invite colleagues to golf outings or entertain them in his home.

But what sustains and propels him to put in such marathon hours? Really, it comes down to wanting to make a difference, he says. Besides, the professional relationships he has built are immensely satisfying, he adds; and it's hard *not* to be inspired by the courage he sees in his patients.

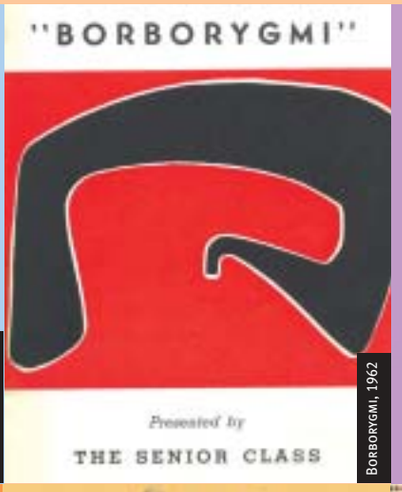
It appears he is in the right place. ■



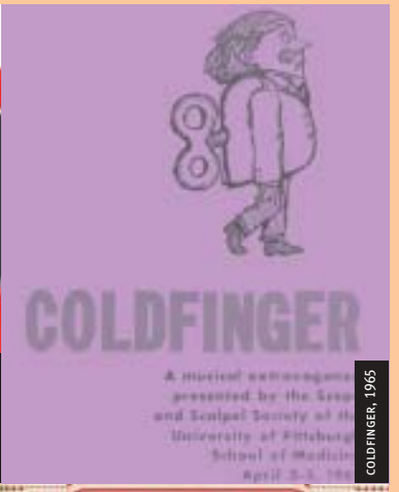
SPRING TONIC, 1956



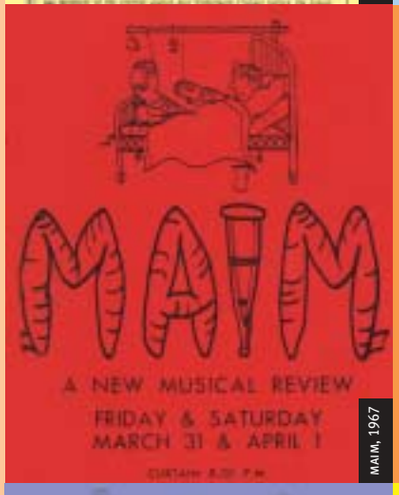
ADIPOSE WRECKS, 1959



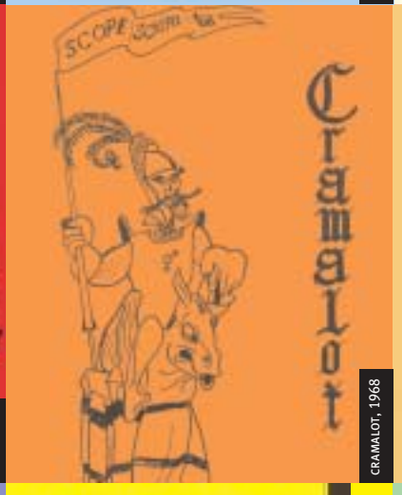
BORBORYGMI, 1962



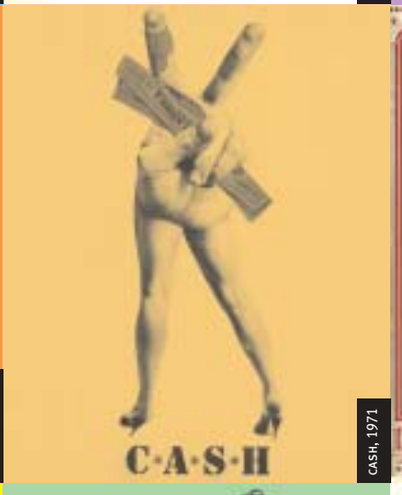
COLDFINGER, 1965



MAIM, 1967



CRAMALOT, 1968

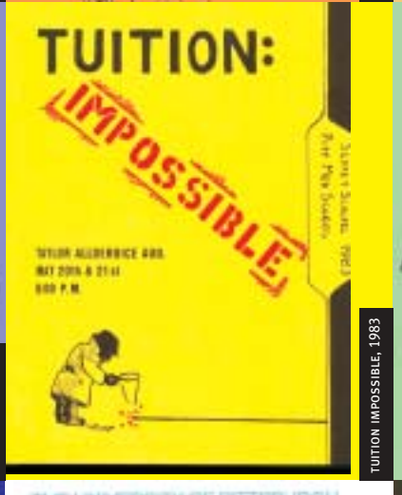


CASH, 1971



MIDAS WELBY MD, 1976

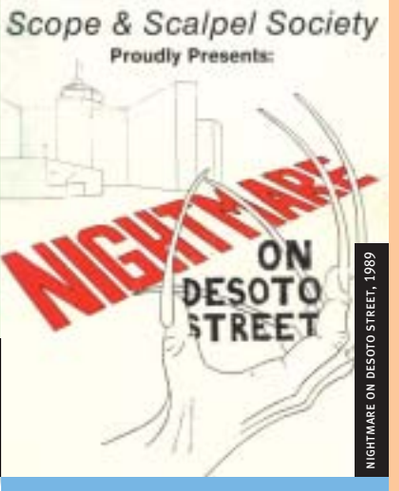

SLIPPED DISCO, 1978



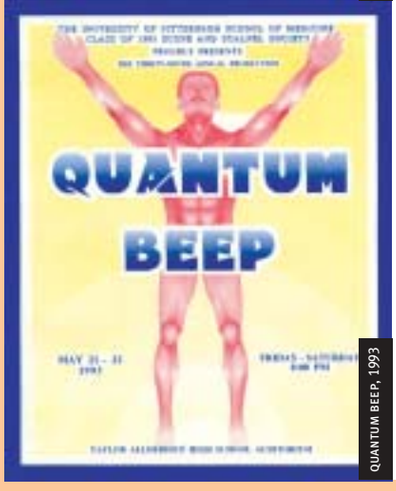
TUITION IMPOSSIBLE, 1983



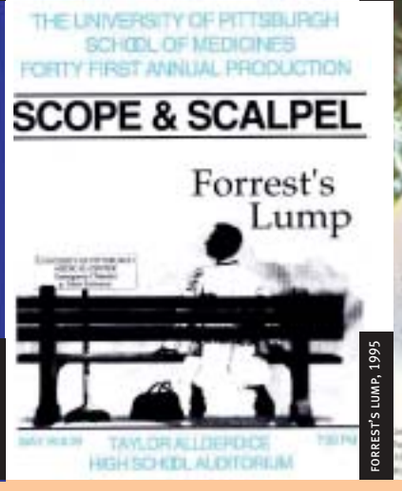
LOST IN SCAIFE, 1985



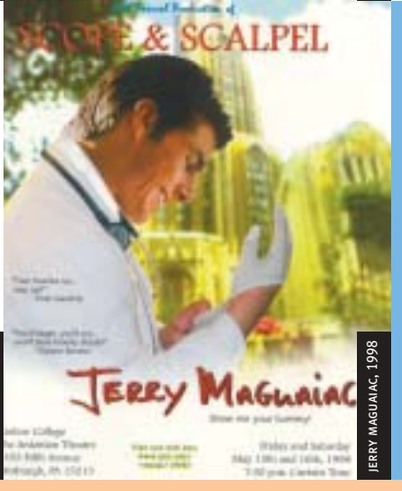
NIGHTMARE ON DESOTO STREET, 1989



QUANTUM BEEP, 1993



FORREST'S LUMP, 1995



JERRY MAGUAIAC, 1998

**There's more where these came from, lucky for us. This must be the longest running show off DeSoto Street.**

***Semper Hilarity, Scope and Scalpelum.***

# CALENDAR

## OF SPECIAL INTEREST TO ALUMNI AND FRIENDS

### PITT MED: ON THE ROAD
**MARCH**
Florida
Topics: Stem Cell Research and Bioethics
For information
Jennifer Rellis
877-MED-ALUM
jrellis@medschool.pitt.edu

### BAHNSON LECTURE
**MARCH 16**
G. Michael Deeb, MD, Speaker
Lecture Room 5
Scaife Hall, 10 a.m.
For information
Kathleen Haupt
412-647-5314
http://www.surgery.upmc.edu

### MATCH DAY
**MARCH 21**
Lecture Room 4
Scaife Hall, noon
For information
Student Affairs Office
412-648-9040
student_affairs@medschool.pitt.edu

### 15TH ANNUAL BLACK BAG BALL
**APRIL 20**
Sheraton Station Square
(Medical Alumni Association sponsored student ball)
For information
Ross H. Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

### STARZL LECTURE
**APRIL 20**
Lecture Room 5
Scaife Hall, 10 a.m.
For information
Kathleen Haupt
412-647-5314
http://www.surgery.upmc.edu

### THIRD ANNUAL PITT MED GOLF OUTING
**APRIL 28**
Quicksilver Golf Course, 8:30 a.m.
Midway, Pennsylvania
For information
412-648-9090 or
golfouting@pittmed.pitt.edu

### ANNUAL ALUMNI DINNER DANCE
**MAY 17**
Pittsburgh Athletic Association
Pittsburgh
For information
Medical Alumni Association
412-648-9090
medalum@medschool.pitt.edu

### SENIOR CLASS LUNCHEON
**MAY 17**
The Twentieth Century Club
Pittsburgh
For information
Medical Alumni Association
412-648-9090
medalum@medschool.pitt.edu

### GRADUATION CEREMONY
**MAY 20**
Carnegie Music Hall, 10 a.m.
For information
Student Affairs Office
412-648-9040
student_affairs@medschool.pitt.edu

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



## GO

**Fresh off an October trip to Boston, Pitt Med: On the Road is driving your way. Expect lively discussions on stem cell research, bioethics, and other traffic-stopping topics. For more information, contact Jennifer Rellis at 877-MED-ALUM or jrellis@medschool.pitt.edu.**

**2002 Destinations:**

**Florida, California, Washington, DC**

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