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OVER THE TRANSOM

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(E. Cerri)
What ever happened to the paperless hospital?

Another reason for a glass of wine.

A mural reduces the need for sedatives.

Mapping memory.

MicroRNA pulled from the junk pile.

Treating the gut with behavioral therapy.

It's all about the nightlife at this summer camp.

Ake Grenvick, a critical care legend.

Robert Yellon builds ears.

A rough introduction to the NFL.

Grim Rea-purr.

FRANK HARRIS ("Camp Sundown," "Japan Honors Sando," and other illustrations) is a 46-year-old artist/illustrator who focuses on caricatures and portraits. Faces often pull him into his work. The face becomes a character, and the character inspires the rest of the piece. "If I can find something that excites me, then the picture just sort of paints itself." Harris says that despite his love of life, a part of him sees it as farcical and absurd. "I think I have a satirical edge that comes through in the artwork."

New York City-based writer SARA GOUDARZI ("Two Kinds of Disease") was born in Tehran and grew up in Iran, Kenya, and the United States. After earning a master's degree in bioresource engineering from Rutgers University, she returned to her first love, writing, receiving a master's in journalism from New York University. "The thing about writing is that I am never stuck in one world," she says. "With nonfiction, as in the case with "Two Kinds of Disease," I'm fortunate enough to get to share a part of someone else's world. With fiction and poetry, I get to create my own."

Not only did Pitt's chair of medicine start smoking for an experiment, he performed a bronchoscopy on himself. (Cover: © moodboard/Corbis, 2007.)
And all that the Lorax left here in this mess was a small pile of rocks, with the one word... "UNLESS."

Whatever that meant, well, I just couldn’t guess.
—Dr. Seuss, *The Lorax*

It is widely assumed that when a new federal administration is installed, health insurance will be made available at a national level to all Americans. The momentum is strong, given that one of every three of us went without insurance for at least some portion of the past year, and that corporate America is increasingly unable to provide benefits without going broke. I worry that the cost of universal insurance will be staggering unless we simultaneously address the many issues that have not only driven the cost of care to a record high, but have given us inadequate bang for the buck. The most pressing of these issues lies in the fact that only half of all adult patients receive treatment for their illness based on scientific evidence, and children fare worse. Thus, we squander half of our payment for health care.

We generally reimburse caregivers for treatment, but not for prevention, even knowing that much of our health care cost is occasioned by smoking, obesity, and other preventable root causes of illness. We practice medicine defensively and expensively—often with unnecessary and inappropriate diagnostic tests—because we fear litigation. Our pharmaceutical industry, beholden to its shareholders, markets “me-too” drugs, at great advertising expense, because paradigm-shifting drugs emerge only infrequently. (With the advent of “personalized medicine,” i.e., prescriptions dictated by a patient’s genome, the economic basis of the industry will become even more challenging.)

As the “boomers” age, more will end their lives in an ICU, the costliest of health care settings. But how many of us wish to spend our last weeks in such a place? Whatever the setting, we continue to make too many errors and have too much inefficiency in the delivery of health care. In the main, this reflects the lack of national standards and lack of a nationally interoperable electronic medical record, as well as the fear of litigation, which causes practitioners and hospitals to obscure rather than to learn from their mistakes. One bright spot is the increasing use of “pay for performance” and “no pay for avoidable errors” approaches, but these schemes are largely experimental, with many challenges as to where the truth lies in complex clinical settings.

Most physicians are paid piecemeal, such that they are more likely to do too much rather than too little. Of course, the huge tuition debt of graduating medical students doesn’t help the cost of care. With a mean debt payoff of more than $200,000 confronting the great majority of American medical students just as they are about to initiate independent careers, it is no wonder that most opt for subspeciality rather than primary care careers—and for wealthy suburbs rather than inner cities or small towns. (We need to offer loan-forgiveness programs on a large scale for graduates who will spend a few years doing what the country most needs—i.e., primary care for the disadvantaged and clinical research to bring the “bench to the bedside” in an era of awesome scientific promise.)

The end result of all of this is that our nation spends a great deal more on health care per capita than any other industrialized country but lags woefully in appropriate and well-coordinated care and timely care; the proportion of citizens who have long, healthy, and productive lives; and the equity with which all of our peoples are treated. In fact, the real issue here is not that we spend too much on health care—maybe 20 percent of our GDP is fine—but that we are getting so little for it. It will not do to address each of the Lorax’s rocks independently and incrementally. The whole mess must now be fixed at once. ... UNLESS.

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

This column also appeared in the Pittsburgh Post-Gazette in November 2007.
Japan Honors Sando

Isamu Sando, professor emeritus of otolaryngology at the University of Pittsburgh School of Medicine, was feted in his native Japan for his lengthy service in the field. In May, he was awarded the Order of the Sacred Treasures, Gold Rays with Neck Ribbon at a ceremony at the Japanese Government Office in Tokyo. After receiving the honor, Sando visited the Imperial Palace, where he had an audience with Emperor Akihito.

Sando, an MD, has served on the faculty of Tokyo’s Nihon University School of Medicine. The award was given in recognition of his work benefiting the Japanese and others. Sando joined Pitt in 1976, becoming a full-time temporal bone researcher and director of the Division of Otopathology. He has contributed to the basis of our understanding of the clinical anatomy of the inner ear, middle ear, and Eustachian tube. —Joe Miksch

FOOTNOTE

Psst, buddy. Wanna buy a medical school?
The year was 1908. The Western University of Pennsylvania had just become the University of Pittsburgh. The unaffiliated Western Pennsylvania Medical College was church-mouse poor. Looking to grow, Pitt bought the med school for a paltry $100,000.

Today, that’ll get you about 50 reconditioned defibrillators and a gross of tongue depressors.

BEATING HEART TRANSPLANT

One of the many pitfalls of transplantation is that organs, when they’re being transported and not performing their duties within the body, can fall prey to damage. A clinical trial led in Pittsburgh by Kenneth McCurry is testing a new device intended to keep a heart pumping en route to the OR.

The Organ Care System (OCS), designed by a Massachusetts company that’s also funding the study, was used to keep a heart beating for nearly three hours before it was transplanted into a 47-year-old Western Pennsylvania man. He was discharged in late April 2007 and is doing well.

McCurry, an MD assistant professor of surgery in the School of Medicine and director of cardiopulmonary transplantation at UPMC’s Heart, Lung, and Esophageal Surgery Institute, says the OCS may greatly improve the health of the transplanted heart, leading to less rejection and shorter hospital stays. —JM
It sounded so promising in the ‘90s—paperless hospitals. Computers promised more, faster, and better information for doctors and patients. But it hasn’t happened. Physician acceptance, high costs, and compatibility problems have kept paper the dominant recording medium in most U.S. hospitals.

At UPMC, Dan Martich (above), vice president of eRecord and chief medical information officer, has led a $200 million effort to leave the paper world behind. With more than 2 million discreet patient records, UPMC’s is among the most-digitized hospital record systems in the country.

Martich, a critical care physician and professor, shared his thoughts on technology and the future of medical records.

On the benefits of electronic records
When the big Vioxx scare happened [Merck’s anti-inflammatory drug was pulled from the market in 2004], within a 24-hour period we had letters out to each of our physicians with a list of their patients who were on Vioxx. Those are things that are just [unheard of] in the paper world—they don’t happen.

On the likelihood of a paperless hospital
I have a phrase, “not paperless, less paper.” I think there’s a need for less paper, but I think a truly paperless physician’s office or hospital is about as practical as a paperless bathroom. You need some amount of paper to mitigate the risks of losing power or losing connectivity. If we don’t plan for those kinds of failures, we’re deceiving ourselves.

On the next frontier in electronic records
The big frontier in electronic medical records is interoperability. That’s the biggest headache. There are over 400 different vended products [such as Cerner Millennium] out there on the market, and they don’t all operate on the same system. Even within the same system, the programming language may be a little different, from even the same vended product, from site to site.

His question for the world
If everyone believes this is the right way to go, that we need electronic records that run cradle to grave for every man, woman, and child, why isn’t it done already? —Interview by Reid R. Frazier

Less Paper Please, Says Dan Martich

A&Q

Next Generation

She’s discovered two diseases since starting here,” Jerry Vockley says of Miao He, a clinical biochemical genetics fellow in the lab of the MD/PhD professor of pediatrics and human genetics. “That’s a good career for most people.”

He, a PhD, played a major role in unearthing a previously unknown enzyme-related disorder that leads to acute liver failure if left untreated. Her work on the topic was published in the July issue of The American Journal of Human Genetics. More recently, she helped identify a cholesterol-synthesis disorder that leaves patients with significant shortcomings in mental and physical development as well as severe skin problems. She’s preparing a paper on this subject for publication.

Amber Barnato, Janet Lee, and Wenjun Wang—Department of Medicine chair Steven Shapiro calls these three “rising stars with the potential for excellence in academic medicine.” They also are the first recipients of the Junior Scholars Award, a $35,000-a-year, two-year grant intended to ease the path to the peak of academic medicine for those with “inordinate family responsibilities.”

Barnato is an MD assistant professor of medicine and health policy and management who studies end-of-life care in hospitals. Lee, also an MD, is an assistant professor of medicine. She is investigating the mechanism by which red blood cell transfusion can result in lung injury in critically ill patients. Wang, an MD/PhD research assistant professor of medicine, seeks to understand the role a transcription factor called Foxp3 plays in melanoma.

Shapiro sought to create the award after arriving at Pitt in 2006 (see profile on p. 18). He says the money essentially buys time. It can be used to hire a research assistant or help with elder or child care. Lightening such duties, Shapiro says, allows an investigator more time in the lab. —JM
**Wine v. Cancer**

An agent common in vegetables and fruits, including black raspberries and red wine grapes, kills leukemia cells in culture while allowing normal cells to thrive.

Spurred by previous reports that identified anti-cancer properties in naturally occurring antioxidants called anthocyanins, Xiao-Ming Yin, associate professor of pathology at the University of Pittsburgh School of Medicine, obtained the most common type, C-3-R.

When his lab group introduced C-3-R to leukemia cells, about 50 percent of them underwent apoptosis, or programmed cell death. At a higher dose, it killed all leukemia cells. Normal cells were unaffected.

Yin's results were published recently in *The Journal of Biological Chemistry*. —JM

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**JUST BETWEEN PEERS**

When Rachel Hess was on fellowship at the University of Pittsburgh's Center for Research on Health Care and considering a junior faculty position there a few years ago, she didn’t know how to negotiate for an academic post.

So she turned to a group of women who did, and eventually she accepted a position at Pitt. Hess is now an assistant professor of medicine.

“This was the group of people who told me what was in the scope of ‘askable’ and what was in the scope of ‘reasonable’ and what was in the scope of ‘a little out there but I could ask anyway.’”

The group is an informal collection of faculty members in the Department of Medicine that goes by the appellation “Research Women.” They meet every few months at swank restaurants near campus. (“We basically hit hot spots that can feed enough people,” Hess confesses.) They share tips on everything from gaining tenure to navigating family leave policy to finding dry cleaners.

The group is a form of “peer-to-peer” mentoring—a place where students and young faculty can find guidance from those at or just past their station on the academic totem pole.

At least one other such grassroots group has popped up on campus. Peer-to-peer is gaining momentum nationally, says Darlene Zellers, director of the Office of Academic Career Development, Health Sciences.

She notes that when young doctors and scientists lean on each other this way—and also seek out more established mentors—their productivity improves, and they have greater success in obtaining grants and getting published:

“When other people take you under their wings, it puts you at an advantage. If you think about it, it’s common sense.” —RRF

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**CLIFFS NOTES: THE CLASS OF 2011**

The Class of 2011 consists of the usual suspects: multitalented women and men who are curious, compassionate, and accomplished. They wouldn’t have been admitted otherwise. That said, a few caught our attention.

The class has a U.S. Military Academy at West Point graduate, foreign languages major Jon Lewis, and a former Army medic, Tara Miller, who was named Noncommissioned Officer of the Year.

Steven Addo-Yobo helped build water towers in Ghana with an aid organization he founded and directed. Tiffany Behringer wrote her thesis at the University of Pennsylvania on the reproductive decision-making processes of Chinese immigrant women. Her work won her the W.H. Rivers prize for most outstanding U.S. undergraduate student research paper.

Gil Hoftman graduated from UCLA. He’d left the academic path for a time to tour with his band. His classmate Timothy Ng started college at 14 and never left. Now 22, Mr. Ng has at least four more years to go. —JM
Appointments

Larry Moreland, the former associate dean for clinical research at the University of Alabama at Birmingham, is the new chief of the Division of Rheumatology and Clinical Immunology at the University of Pittsburgh. Moreland, an MD who also held an endowed professorship and directed the Pittman General Clinical Research Center and the Arthritis Clinical Intervention Program at UAB, helped establish the first FDA-approved biological agent for the treatment of rheumatoid arthritis.

He joins a division that was recently ranked 10th of its kind in the United States by U.S. News and World Report.

Yoel Sadovsky is the new science director of the Magee-Womens Research Institute. He's also a professor and vice chair for research in the Department of Obstetrics, Gynecology, and Reproductive Sciences. Sadovsky comes to Pittsburgh from Washington University in St. Louis, where he served as director of the Division of Maternal-Fetal Medicine and Ultrasound.

Sadovsky's research explores the molecular mechanisms that determine placental differentiation during human pregnancy. “The placenta is the communication center,” he says. “How does it function during pregnancy? What are the potential injuries to the placenta that may adversely affect the developing fetus? How can they be overcome, and how can they be prevented from causing diseases?”

Sadovsky, an MD, says that the Magee-Womens Research Institute appeals to him because it encompasses all elements of women's and newborns' health—from the molecular and biochemical aspects of prenatal development through birth and beyond.

“It’s a really unique place in that way,” he says.

The new chair of the Department of Neurological Surgery, Amin Kassam, has been in the School of Medicine for nearly a decade. He had held the position in an interim capacity, beginning in 2006, in the wake of L. Dade Lunsford’s decision to step down to spend more time in the clinic.

Kassam, an MD, also directs the UPMC Center for Cranial Nerve Disorders and codirects the Center for Cranial Base Surgery. His surgical career has focused on cranial nerve disorders. In recent years, he has led the development of endonasal cranial skull base surgery, which allows for the removal of tumors, pituitary lesions, and vascular anomalies through the nostrils. This innovative procedure has garnered Kassam international recognition, as has his experience with microvascular decompression surgery, a procedure that relieves facial pain, throat pain, tinnitus, and deep ear pain. —JM

Standing in the MRI room of Children's Hospital of Pittsburgh of UPMC is like being underwater. Minus the water.

An octopus, some angelfish and starfish, and a slew of other painted creatures drift along blue walls. Colorful coral completes the feel. When the lights are dimmed for an MRI procedure, the room seems to come alive. The Indiana University of Pennsylvania Art Education Student Association created this peaceful aquatic world for young patients at the request of Children's radiology department. The artwork relaxes children and has reduced the need for sedatives.

—Matt Minczeski
MEMORY MAPS

On the other side of the glass from a bank of computers, all that was visible of Greg Siegle were the soles of his shoes. The rest of him was firmly ensconced in a functional magnetic resonance imaging (fMRI) machine in UPMC Presbyterian. The computers collected data in real time and were creating a map of his brain at work.

Siegle wasn't a patient, however, and no doctor was planning to review the images generated by the scan. Rather Siegle—a PhD professor of psychiatry in the School of Medicine—slipped into the fMRI to help California-based artist Deborah Aschheim, whose work has long focused on the brain and notions of how the organ creates and organizes memory and emotion.

Aschheim, recently an artist-in-residence at the University of California, San Francisco, began to collaborate with Siegle in 2006 after he and other neurologically inclined faculty saw Aschheim's installation art piece called “On Memory” at the Mattress Factory museum on Pittsburgh's North Side. In the piece, she recreated maps of her own memory-related neuronal activity in plastic, light, and electronics.

As Siegle lay supine in the fMRI, he was being shown images from Aschheim's old family movies. (He would also view his and those of two colleagues on the project.) Aschheim hopes to use the resulting scans as the basis for an as-yet-undetermined artwork.

"People respond to my movie, and you can see that the movie triggers memories of their own," Aschheim says. "It's interesting to see which areas of the brain light up. In a way, science and medicine might be able to help you understand your feelings differently than you do yourself."

—Joe Miksch

Photo by Owen Smith
“JUNK” GENETIC MATERIAL COULD DECODE CANCER  |  BY REID R. FRAZIER
There are few decorations in Bino John's office in the University of Pittsburgh's gleaming new Biomedical Science Tower 3 in the heart of Oakland. A row of Russian matryoshka dolls—from his wife's home country—sits atop a bookcase filled with biology textbooks. Only one picture graces the room. The photo, on a desk next to a window overlooking Fifth Avenue, shows John's mother, Susamma Varghese, smiling at the camera.

The photo serves as a reminder to John, an assistant professor of computational biology, of why he comes to work every day. Varghese died in 2005 of liver cancer. She was 54.

"I tell you, only when you see it, only when you are there to experience it, do you know how bad [cancer] is. This is the worst thing that ever can happen to you. It breaks you down to nothing."

When his mother got sick, John was finishing his postdoctoral work at New York's Memorial Sloan-Kettering Cancer Center. He had helped develop a computer model there that would predict where on the genome tiny strands of genetic material called microRNA (miRNA) might interact or bind.

John flew back home to his native India to be with Varghese during what turned out to be the last week of her life.

"That one week of suffering that I saw, I was completely helpless. There was nothing I could do. Nothing medicine could do. I decided, 'Cancer is the way I'm going to go.'"

John shifted his research focus to looking for links between cancer and miRNA. These are small strands of genetic material, 22 base pairs of nucleotides long, as opposed to 500 to 1,000 for a common strand of ribonucleic acid, or RNA. Because they are tiny, scientists widely dismissed them until 2000, says John.

Their discovery has helped overhaul the conventional thinking about genetic transcription. The traditional wisdom, as handed down in biology textbooks for the past few generations, is that DNA encodes RNA, and RNA gets translated into protein in organelles called ribosomes, the cell's protein factories.

Turns out, the vast majority of DNA—about 95 percent of it, actually—doesn't code for protein. What role does this DNA serve? Scientists didn't know. They divined that it was probably junk—kind of like stacks of untouched files in a crowded office.

Biologists initially lumped miRNA in the junk pile—then discovered the tiny RNAs played a major role in regulating gene expression. The miRNA can latch onto a strand of messenger RNA and prevent it from being translated into proteins. Jam the signals to the protein factory, and the cell must improvise to survive, resulting in genetic diseases such as cancer.

Biologists noticed that in cancer cells, miRNA levels were often different than in healthy ones, so many began to look for an miRNA signature in cancer.

They also found that different types of cancers presented with different types of miRNA. If they could develop a molecular profile for cancer, they could detect cancer earlier and with more precision.

There's a "but" in here.

"There's a big catch with microRNA," says Patrick S. Moore, director of the Molecular Virology Program at the University of Pittsburgh Cancer Institute and Pitt professor of molecular genetics and biochemistry. Along with his wife, fellow UPCI researcher and Pitt professor Yuan Chang, Moore runs a lab devoted to understanding KSHV, a virus they discovered in 1993 that causes Kaposi's sarcoma. (AIDS patients frequently contract this cancer.) Moore and Chang are collaborating with John to look for proteins controlled by miRNA in KSHV.

"It's very hard to know what [miRNAs'] targets are—of the 3 billion base pairs in the human genome, which part are they going to bind with?" says Moore.

As John explains it, here's the problem: In a perfectly formed RNA-RNA interaction, the RNAs match up predictably. But miRNAs interacting with messenger RNAs play by a different set of rules. Figuring out where they will bind is like a really, really hard Sudoku puzzle.

That's where John's work in computational biology comes into play.

He has developed an algorithm for finding the targets of miRNAs and has collaborated with Moore and Chang to validate this approach in KSHV.

"Bino's been at the forefront of a field that's exploding," Moore says.

Scientists have identified roughly 500 miRNAs. John thinks there are thousands of other tiny RNAs out there, an intimidating thought for anyone who wants to figure out cancer.

"As you look deeper and deeper into the cell, conventional thinking does not hold. There are patterns we can't explain at this point based on our understanding of DNA," he says.

"The lesson we continue to learn is the cell has a lot of surprises."
Kids and teens with pediatric-onset inflammatory bowel disease (IBD) suffer from diarrhea and significant abdominal pain. They often miss school. Puberty can come later than usual. They might not want to share the details of their condition with peers.

IBD kids—whether they suffer from Crohn’s disease or ulcerative colitis—can be isolated from their peers, and isolated kids can become depressed. About a quarter of youngsters who develop IBD suffer from depression developed concurrently with IBD.

By way of comparison, 7 to 10 percent of all 10- to 20-year-olds are depressed.

Typically, doctors treat IBD with anti-inflammatory medicines, steroids, and immunosuppressives. Eva Szigethy, an MD/PhD assistant professor of psychiatry and pediatrics in the University of Pittsburgh School of Medicine, is in the process of developing a behavioral treatment that addresses IBD-associated depression. It turns out that her method also may reduce the severity of IBD symptoms.

“This is a truly remarkable result,” says David Perlmutter, Vira I. Heinz Professor and chair of pediatrics at Pitt. “This is one of the few and may be the only example of behavioral therapy having a clear clinical impact on organ injury.” Perlmutter is an MD who specializes in pediatric gastroenterology and nutrition.

About six years ago, Szigethy, who also is medical director of the Medical Coping Clinic of the Inflammatory Bowel Disease Center of the Division of Gastroenterology at Children’s Hospital of Pittsburgh of UPMC, visited with John Weisz, a renowned expert on cognitive behavioral therapy (CBT) then at UCLA.

CBT asks patients to develop their ability to differentiate things they can control from things outside their mastery. It trains the mind to accentuate the positive and ignore uncontrollable negative events. Could it help children with IBD?

“This whole theoretical model is a very good fit for physical illness. Being diagnosed with IBD is outside kids’ control but learning how to cope with stress can positively alter disease course,” Szigethy says. “It helps people ask, ‘What am I going to do differently? And, ‘How am I going to change my thinking if I have to accept I’m going to have this illness?’

The fact that CBT is drug-free also appealed to Szigethy. “These kids already have a very high burden of medication,” she says. “Their gastrointestinal tracts are also affected by the disease, so they might not absorb the medicine well.”

In 2004, Szigethy was the first author on a paper in the Journal of the American Academy of Child and Adolescent Psychiatry that bore her suspicions out: CBT seems to work for IBD kids. She found significant improvement in depression among her subjects; they reported improved quality of life and developed a better perspective on managing the illness.

The critical thing about this study, says Szigethy, is that “a focus on the child’s illness perception/experience was integrated into the CBT program.” When kids have negative perceptions of their illness, they have more difficulty coping. That, in turn, leads to a more arduous disease course, she notes.

Not long after Szigethy completed the study published in 2004, she undertook a randomized trial. Of the 41 participants, 22 received CBT in addition to their IBD medication. The remainder received IBD medication alone. Depression was comparatively lessened in the CBT group. She published the resulting paper in 2007.

The work uncovered one more piece of good news: “When we looked at the kids six months out, the CBT group had significantly less IBD severity,” says Szigethy.

She developed a handbook to guide mental health professionals to engage in the therapy with youth suffering from IBD. Parents get training as coaches, but kids do the CBT “work” themselves, so they aren’t reliant on perpetual therapy to guide them through rough patches. Kids learn how to relax and do self-hypnosis, modify their perception of the illness, and enlist the help of others—including family and friends.

The National Institutes of Health recognized Szigethy in September with a prestigious New Innovator Award worth $1.5 million to study the neurobiological and immunological effects of CBT intervention in the same population.

She says, “It’s very exciting that a psychological intervention—teaching kids stress management techniques—could potentially affect immune system function to the degree that they can actually fight the disease better.”
there are two kinds of disease in the vaccine world: those that are, relatively speaking, a piece of cake to fight with vaccines and those for which creating immunity seems impossible.

"Roger Rank used to tell me all the easy vaccines have been developed. All the ones that are left are much more difficult," says the University of Pittsburgh’s Toni Darville of her mentor Rank, of the University of Arkansas.

The easiest vaccines—such as mumps or tetanus—have more or less been rolled out. Other infections have kept scientists laboring away in their labs for years. Darville is determined to formulate a vaccine for a tough one—chlamydia. Caused by the bacterium Chlamydia trachomatis, it is the leading cause of involuntary infertility worldwide.

Darville, a professor of pediatrics and immunology, uses the mouse model of chlamydial genital infection, which Rank developed, for her work investigating how to protect people against the infection. Darville worked with Rank from 1993 until this past August, when she moved to Pittsburgh and became chief of the Division of Pediatric Infectious Diseases at Children’s Hospital of Pittsburgh of UPMC.

"The easiest vaccines—are mumps or tetanus—have more or less been rolled out. Other infections have kept scientists laboring away in their labs for years. Darville is determined to formulate a vaccine for a tough one—chlamydia. Caused by the bacterium Chlamydia trachomatis, it is the leading cause of involuntary infertility worldwide.

"Boys don’t have a big problem with it. They may experience some mild penile discharge and mildly painful urination," says Darville. "But in girls, over time and with repeated infections, this organism ascends from the lower genital tract to the upper genital tract to the fallopian tubes and causes scarring, which can lead to chronic pelvic pain and infertility.”

The peak incidence of infection falls among young people between 15 and 20 years old, says Darville.

"If you look at various populations of sexually active teenagers, the infection rates range anywhere from 7 to 20 percent.”

As we age, however, it seems that some immunity against the infection develops. Scientists are not exactly sure of the mechanism behind the immune system boost, though they suggest early exposure to the bacteria could trigger immunity changes. So could alterations in hormonal status and the lining of the uterus and fallopian tubes.

"That gives us hope that we could develop a vaccine that could perhaps help prevent infection, but at the very least develop a vaccine to prevent disease due to this organism," Darville says.

Yet unlike measles or chicken pox, in which the infection itself induces an immune response, contracting chlamydia doesn’t lead to protection from re-infection.

Scientists typically develop vaccines by taking proteins of a disease-causing organism and injecting them into a human to induce antibody production.

The antibodies help the immune system conquer the interloping bug. The immune system remembers and recognizes that particular bug, and the next time the invader comes around, the body is ready to attack.

Although they can help prevent re-infection, antibodies of some diseases—like chlamydia and herpes, as well as viral infections such as HIV—are not completely protective. In these cases, scientists can’t just take an immunogenic protein, put it in a syringe, and vaccinate a person.

One trick, Darville explains, is to add adjuvants. These agents stimulate the immune system without having any effects in and of themselves. Using an adjuvant with a weakened strain of chlamydia could be the key to preventing re-infection. But adjuvants can make vaccines expensive to manufacture.

Darville’s colleague, visiting assistant professor Catherine O’Connell, a bacteriologist who also came to Pittsburgh from the University of Arkansas, has developed weakened, or attenuated, strains of chlamydia. She managed this by removing the resident plasmid (a DNA molecule able to self-replicate) from a strain of chlamydia that infects mice. When researchers inject mice with these chlamydia strains, they develop the infection but not the disease. With this model, Darville and O’Connell can use mutant strains to determine the characteristics of an exclusively protective immune response to chlamydia infection.

"That gives us a road map with which to say, ‘OK, this specific response occurs, and that’s a desirable response,’” Darville says.

The two scientists are hoping a similar approach with strains of the bacteria that cause genital tract disease in humans will also illuminate protective immune responses. Such understanding could become the basis for a human vaccine—one that industry could more easily and cheaply manufacture than those that require adjuvants.
Before we head over to the South Side of Pittsburgh and Seong-Gi Kim's lab, a brief visit to England is in order. In 1890, a pair of Charleses—Charles Roy and Charles Sherrington—proposed that neural activity could be correlated with increased blood flow to the active part of the brain. The harder nerve cells work, Roy and Sherrington's research suggested, the greater their need for oxygen and, therefore, the greater the need for blood at the site of increased neural activity.

This discovery, coupled with technological advances made over the course of the next century, has given the scientific community a powerful tool with which to see what's going on in the brain without cracking the skull: functional magnetic resonance imaging (fMRI). Essentially, fMRI uses powerful magnetic fields to monitor vacillations in blood flow. Hemoglobin, the iron-containing oxygen transporter in mammalian red blood cells, repels magnetic fields when oxygenated and is attracted when deoxygenated. The resulting three-dimensional images give a snapshot of a brain at work.

Or do they?

The answer to that question passes judgment on the accuracy of thousands of research programs attempting to understand how we think and what is happening when our brains don't behave in healthy ways.
Since the early 1990s, when the first fMRI machines were built, there's been some controversy over whether the technical capabilities of the device and the techniques doctors use to interpret fMRI results truly measure what they are thought to measure. It’s true that fMRI doesn’t measure neural activity directly, so maybe there is some chance that an apples-and-oranges thing is going on here. It’s also possible that different areas of the brain oxygenate and deoxygenate differently, skewing comparisons. And though the most powerful fMRI machines can measure activity in a physical space smaller than a millimeter, even with the latest technology, images aren’t captured often enough to plot neural activity in real time. Neural activity takes place on a submillisecond timescale.

At the University of Pittsburgh’s McGowan Institute for Regenerative Medicine on East Carson Street, Kim is in the midst of a decade-plus-long effort to refine fMRI technology. The essentials of the professor of radiology and neurobiology’s lab consist of an fMRI machine and a cadre of cats. With these tools, Kim seeks to find out whether fMRI indeed depicts with precision specific areas of neural activity. In short, do the places that light up on a scan truly show where a given thought happens?

Kim is mapping bunches of neurons called cortical columns to find out. To perform his cortical-column mapping, Kim, a PhD, sedates the felines to calm them, though they remain conscious. Images of black-and-white bars within circles projected in front of the cats elicit neuronal activity, sort of a kitty kaleidoscope. Before fMRI, scientists first mapped cortical columns in live animals by using voltage-sensitive...
dyes and a video camera. That was around 1986. Later, the preferred technique was to measure the light-absorbing properties of hemoglobin. These approaches limited research conclusions, considering the scientists could see only the uppermost layers of the exposed animal cortex.

LEFT: Thin horizontal slices of a cat’s cortex are depicted via fMRI to a resolution of 78 microns. The dark areas, both spots and lines, are veins. The vertically oriented slices on the far left provide a detailed map of a very small portion of an active cat cortex. Kim’s lab can capture such high-resolution images by using an experimental 9.4 Tesla fMRI scanner—most commercially available scanners operate at 7 Tesla or less—which enables the machine to detect blood oxygenation changes in extremely small vessels. Kim’s scanner’s magnetic field strength is about 188,000 times stronger than the Earth’s.
Using fMRI, Kim isn’t bound by such constrictions. He can go as deeply into a cortical column as he likes, thanks to the noninvasive nature of the technique. He’s eager to learn whether the fMRI signals that have been thought to correlate with neural activity on a large scale (more than a millimeter) are also detectable on a submillimeter scale. In large vessels, there’s more blood fueling neural activity and, therefore, more detectable hemoglobin. Capillaries, the focus of smaller scale detection, carry much less blood. Using statistical analyses, Kim can greatly reduce the interference caused by signals from large blood vessels and focus on the little things, which in this case are the big things.

So does fMRI tell doctors and other scientists what they think it does? Right now, science is certainly seeing the neighborhood of neural activity with fMRI, Kim will attest. His work will help researchers get to a precise address.

What’s at stake? Science’s ability to unravel thought itself.
BELOW: The cats Kim studies watch these lined circles. The red arrows indicate the direction in which the images oscillate.
The DRIVE
The year that Steven Shapiro began his pulmonary fellowship at Washington University in St. Louis—1986—three of the five new fellows were MD/PhDs. Wash U, as it is informally known, is considered a biomedical research powerhouse, and these three new physician-scientists each had the aura of a first-round draft choice entering the big leagues. With their PhDs, they seemed to bring a lot to the table, including years of experience in the lab. Great research was expected of them in this competitive field of academic medicine.

Shapiro was not one of these three, however, which is not to say that he was a slacker.
Shapiro was studying human lung tissue the way that climatologists study tree rings or Antarctic ice cores.

infectious diseases to cardiology, plus an enormous amount of research. Traditionally, medicine is a medical school’s flagship department. Its stature helps to bolster that of all the other departments and of the school as a whole.

It’s a pleasant summer day when the elevator on the 12th floor opens to reveal Steven Shapiro lingering in the hall. He welcomes a few third-year medical students as they arrive. A few minutes later, Shapiro, the Jack D. Myers Professor and Chair of Pitt’s Department of Medicine since arriving from Harvard in 2006, presides over a conference table gathering of eight of these students and one large plate of cookies.

In a pastel dress shirt and tie, Shapiro is broad-shouldered enough to occupy a significant amount of space beneath the basket. In a group like this—with medical students more than two decades his junior—he comes across as a sort of benevolent coach. He’s quick to laugh and wants the students to reciprocate. He’s not in a hurry. The students are wrapping up a semesterlong clerkship in internal medicine, and they are here today for the last of a half-dozen or so grand rounds with the chair of medicine. Instead of presenting case studies, Shapiro uses this last session for his career talk.

He wants to hear what the students see in their futures after what was, for most of them, their first sustained contact with real patients.

“I kind of like surgery, but the hours...” says one young woman.

“You’ve got to love to cut to do surgery,” says Shapiro.

“I want to have kids, I know,” says another. “But I don’t know how to do this—to get a job where I can pick up the kids after school. How old will I be when I can request that kind of time?”

Shapiro reassures her that, though there are challenges to having a family and a medical career, it’s getting easier all the time, even in some residency programs.

He says, “One of the little things we did this year when I took over is that we changed our Department of Medicine faculty meetings [from 5–6:30 p.m. to 4:30–5:30 p.m.] so that everyone can go and get kids from day care before six o’clock. I got e-mails and people thanking me—all women. Not one man. I also got grief—mostly from men in clinic, saying, ‘I can’t get out at 4:30. I’m working.’

“We’re also funding three grants for [faculty members] who are rising stars at a critical stage in their careers with unusual obligations. By and large, that is women with children.”

“I’m M D/PhD,” says one medical student. Then, a bit sheepishly, he admits, “I want to do the trifecta. I want to be in the lab, but I want to be clinically involved, too. And teach.”

Shapiro is galvanized by their enthusiasm. He talks about how their role models may change as they go through their training. They may find great clinical mentors in the hospital, as he did, then encounter terrific bench scientists in the lab.

Shapiro was captivated by the lab work. Now, he annually spends about six to eight weeks doing clinical work in pulmonary medicine. He also regularly reviews cases with residents and interns.

Robert Senior, a professor of medicine at Wash U who was Shapiro’s primary mentor during his pulmonary fellowship, says that Shapiro’s eagerness for science showed immediately when he was a fellow. He developed a research project to try to understand the development of elastic fibers in the lung. (This elastic tissue is vital to the structure and function of the lung. When it breaks down, you get emphysema.) He obtained human lung tissue from people at all ages and developmental stages. He examined them for trace amounts of radioactive isotopes that were known to be in air pollution in specific years to determine when this elastic tissue had formed. He identified an amino acid in the lung that changes its structure over time, indicating its age.

This was totally novel work, says Senior. Shapiro was studying human lung tissue the way that climatologists study tree rings or Antarctic ice cores to date climactic changes. It was published in the prestigious Journal of Clinical Investigation, and it remains an important study of the topic to this day.

“Basically, what Steve showed was that the elastic fiber is extraordinarily stable in a normal lung,” says Senior. “To a large extent, what you have in midlife, or when you are even older, are the same fibers that you started out with.”

This is no esoteric question. In a normal lung, countless tiny air sacs clustered together at the end of your bronchial passages expand and contract with each breath. In emphysema, the thin walls between these little grape-like sacs break down as the elastic tissue degrades—the spaces enlarge and the lung loses elasticity.

At Wash U, Shapiro began a careerlong interest in chronic obstructive pulmonary disease. COPD, as it is known, refers to a combination of diseases that cause difficulty with breathing—mainly emphysema, chronic bronchitis, and, in some cases, asthma. It is the fourth leading cause of death in the United States.

Approximately 90 percent of those who suffer from COPD are smokers or past smokers. In his zeal for answers, Shapiro actually became one of them for a few months.

He had what he thought was a great idea for an experiment. All that was required was a nonsmoker willing to become a smoker. If you have any sort of conscience, there’s only one person you can ask to do that. This was about 15 years ago, when he was a young, invigorated assistant professor at Wash U.
Institutional review boards weren't so restrictive back then, Shapiro says with a laugh.

Shapiro threaded a fiber-optic bronchoscope into his own lung. He maneuvered the flexible, camera-equipped scope through the mouth, delicately negotiated the larynx, then continued straight down the trachea and made a sharp turn into one nice, pink lung. Next, he used the attached syringe to spray a good 20 ounces of saline into his lung. Then, he suctioned it all out. The saline was now swarming with Shapiro's macrophages—millions of white blood cells that he believed would tell him interesting things about the progression of COPD.

His goal was to isolate the RNA from these macrophages, then to become a smoker, repeat the procedure, and see which genes were “switched on” when a nonsmoker became a smoker. This is an important question. Macrophages are the immune system’s foot soldiers. They devour foreign matter, microorganisms, cellular debris, and abnormal or old cells. They are a key step in the body’s targeted immune response because they present antigens to T cells, essentially showing the killer cells what the target looks like. Perhaps the toxins in cigarette smoke are responsible for activating genes in these macrophages that cause the destruction of lung tissue seen in COPD.

The experiment was kind of a bust, Shapiro says. Nowadays it might reveal more, because we’ve sequenced the entire human genome and could much more easily learn which genes are made active by smoking and what those genes do. He admits you could also probably learn just as much by comparing a large enough number of smokers and nonsmokers. But the experience did a few things for Shapiro: One, it got him to thinking very seriously about the macrophage and the limits of what he knew about genetics and molecular biology. And two, it gave him an enormous amount of sympathy—empathy, actually—for smokers who struggle to quit. He calls nicotine the most addictive substance known to man.

“Forget my morning coffee,” says Shapiro of those three months before he quit. “I wanted my cigarette. I swear I had original thoughts about projects I’d been working on for a long time.”

“He will sort of go where the good questions take him,” says Senior, recalling Shapiro’s self-experimentation, “and if it means he’s the guinea pig, he’ll do it. He has an incredible eagerness to learn things.”

Senior’s lab had been interested for some time in enzymes that these macrophages produce. Enzymes are powerful molecules that
break down specific types of proteins when they come into contact with them. Shapiro began to wonder whether a macrophage enzyme could be involved in the tissue damage that results in emphysema.

This was a bold question, because there already was a long-standing scientific explanation for emphysema.

Since the 1960s, doctors knew that patients with a condition called alpha-1 antitrypsin (AAT) deficiency often suffered terribly from emphysema, and they didn’t have to smoke much to get it. AAT was known to inhibit a destructive enzyme called neutrophil elastase, which cells called neutrophils produced. For decades, the obvious conclusion was that neutrophil elastase damaged lung tissue by breaking down the elastin. If you had enough AAT to inhibit the action of the enzyme, you probably wouldn’t get emphysema. People with AAT deficiency, however, were very susceptible to emphysema because they didn’t have the molecule that would inhibit it. This was dogma.

But something about it didn’t make sense to Shapiro.

There were actually rather few neutrophils in the lungs; macrophages were the most plentiful immune cells there. Could those few neutrophils produce enough neutrophil elastase to cause significant damage? Wasn’t it likely that macrophage enzymes were involved?

To test his theory, Shapiro did what no pulmonary scientist had ever done—he learned how to make a genetically altered mouse. This involved some of the most cutting-edge molecular biology techniques available at the time: tools that nobody anywhere in the field of pulmonology was using. Shapiro went into the lab of Tim Ley, a well-known oncologist at Wash U, to figure out how to tease apart the relevant genes.

“He saw the future,” says Senior. “He saw the importance of molecular biology, genetics, and the value of being able to manipulate genes to learn things. And nobody in the pulmonary division had those skills.”

McGarry Houghton, an M.D. and now a Pitt assistant professor of medicine, was a fellow in Shapiro’s lab at Wash U and has worked with him ever since. As Houghton tells it, Shapiro managed to get a bench space about the width of his shoulders in Ley’s lab, but he did a lot with it. (It’s a bit like occupying space beneath the basket but with less chance of taking an elbow to the nose.)

“He cloned [the gene for] this enzyme called macrophage elastase,” says Houghton. “He wasn’t even sure if it actually existed. He found it, he sequenced it, and he made a mouse that didn’t have it.”

Shapiro made a knockout mouse—one that couldn’t make the enzyme macrophage elastase. Then he devised an experiment that exposed this mouse to cigarette smoke—the knockout mouse didn’t get emphysema. Normal mice that were exposed to smoke did get emphysema. Clearly, macrophage elastase was important in the progression of emphysema.

In the pulmonary arena, says Senior, Shapiro “was the first person who put together the idea [to make] a gene-altered mouse, expose it to smoke, and see how it would affect lung injury.”

His discovery changed how people thought about lung injury, says Houghton: “That was in science in 1997. The modern view is that it’s not one cell or one enzyme, because we know these cells work together, and these enzymes all work together.”

Shapiro says that he broke one of the cardinal rules of getting ahead in the business of academic medicine. His transgression: He was happy. He was completely content.

“Physician-scientists are working so hard to succeed,” he says, “they often forget what an honor it is to do academic medicine.”

Since 2001, he’d been the Parker B. Francis Professor of Medicine at Harvard University and chief of the pulmonary division at Brigham and Women’s Hospital, surrounded by terrific scientists and colleagues.

“He assembled a very good multidisciplinary group here, ranging from genetics to animal models to human studies,” says John Reilly, an associate professor of medicine at Harvard who became the interim director of the pulmonary division when Shapiro left. He says the group was something special.

“In the type of group that Steve set up,” Reilly continues, “we could have our genetics guy here say, ‘Gee, we have this study that we’re just completing, and it makes it look like gene A is more common in patients with COPD, and nobody has ever reported that before.’ The question is, ‘Why would it lead to susceptibility to develop COPD?’ Steve can then take that and, in his mouse model, knock out that gene and see what it does in his emphysema model in mice. He can begin to do his experiments to define not only is the gene associated with the disease but why is it associated with the disease, which is the next step in developing therapies to treat the disease.”

Shapiro says that he interviewed for the job in Pittsburgh “to be polite,” which isn’t all that unusual. Good scientists get recruited all the time. And it’s tough to say, “No, thanks,” to a flattering invitation, especially when you have friends and colleagues at the institution in question, as Shapiro did in Pittsburgh.

“The people who answer ads are not the Steve Shirapors,” says David Perlmutter, who became friends with Shapiro (on and off the court) when they were both at Wash U.

Perlmutter is now Pitt’s Vira I. Heinz Professor and chair of pediatrics, as well as the chief physician and scientific director at Children’s Hospital of Pittsburgh of UPM C.

“I was thrilled he was going to look at [the job], but I knew that wouldn’t be enough. We were going to have to go get him.”

At first, Shapiro felt it wasn’t a good time for him to make a change. But the more he learned about Pittsburgh, the more he thought it was too good to pass up.

“I wouldn’t have taken a department chair job anywhere else,” he says. “I actually wouldn’t look at any others except for this one.” Right now, he says, there are very few academic medical centers that have it all going for them—strong scientists, dedicated teachers, excellent patient care, the physical infrastructure of top-notch hospitals, and profitability.

“The relationship between the hospital and the University is really special here,” he says. “You don’t see it anywhere else.”

Perlmutter calls this relationship “the cycle of life” in academic medicine, saying that Shapiro discovered “that the cycle of life is as good as it gets here. We’re expected to do a great job clinically, and we are expected to, in doing that, help the hospital make money to feed our education and research programs. And that cycle of life is administered here in a way that is really appealing to the department chairs. I don’t know of a place like it.”

For Shapiro, the emphasis on patient care is enormously gratifying:

“If a patient calls one of our clinics with a complaint, they get seen within three days, and that’s unheard of in medicine, even in private practice. But we know this is true because there is a ‘mystery shopper’ who calls all our clinics, documents the call, the time, and the wait.”

At Harvard, colleagues like Reilly and
S hapiro says that his lab has been more productive since downsizing and moving to Pittsburgh.

Remember the neutrophil? The immune cell famously and somewhat erroneously blamed for emphysema since the 1960s? Shapiro and Houghton are finding it can promote tumor growth in lung cancer. This is news. Researchers have long known that neutrophils could be found within a tumor, but what they were doing there has been misunderstood until now.

"We always thought that the macrophages and the neutrophils were your defenses to go and kill this tumor, which doesn't really turn out to be true," says Houghton. "You'd think they were going and trying to fight this thing, and some of the lymphocytes probably do. But in the model that we use, the neutrophil is actually being recruited by the tumor itself. The chemokines—the signals that tell the neutrophil to go to this place—are being released by the tumor."

The neutrophil, Houghton says, is adding things like neutrophil elastase to the tumor. But this enzyme isn't degrading proteins there, as scientists have long believed.

"A tumor cell with a little neutrophil elastase will grow at a more rapid rate," says Houghton.

Shapiro's team published on the tumor's neutrophil-recruiting abilities in a 2006 Oncogene. Now they are preparing to submit a manuscript describing the role of neutrophil elastase in promoting tumor progression.

"This is going to be big news," says Shapiro. "People were right all along, neutrophil elastase is very important. They just had the wrong disease. It is lung cancer not COPD."

"There's still a lot of misunderstanding of what the neutrophil does," says Houghton.

A lot of people think they are just kind of there. Nobody, I think, would imagine that they do such important things or that they impact tumor growth so drastically.

This kind of work is a perfect example of Shapiro's scientific instincts, says Houghton. "I just think he's kept his eyes open to what his data has shown him, and he's followed the data. He hasn't just ignored these interesting findings that might lead him in a different direction.

"It's really rare for a pulmonologist to study lung cancer. It's really been left to the oncology groups."

Another research project originated soon after Shapiro arrived in Pittsburgh, when he was asked to write a grant on asthma with Bruce Freeman, Pitt professor and chair of the Department of Pharmacology. His schedule was already jam-packed, and the molecular basis and pathophysiology of asthma were kind of outside of his area.

"I said, 'I'll do it, but I've got nothing,'" says Shapiro.

"That's one of the things that impressed me," says Freeman. "He was spending his full day learning about the people and the new aspects of his job—same with myself, because I'm a new chair—and we were getting up at three or four in the morning to do our research experiments. They'd toil in the lab during the day and pore over data in the evenings. They began to see in mouse models that the initiation of asthma was directly tied to these macrophage enzymes.

"It turns out that their role is much more interesting than we ever thought," says Shapiro.

He expected to find that they degrade the structure of lung tissue and contribute to the thickening of airways in asthma. Much to his surprise, they found evidence that these MMPs appear to regulate the actual initiation of asthma.

"What we turned in," he says, "was a fantastic grant where we found that one of the MMPs we study is critical for the development of a special cell that prevents asthma."

"We have some fresh ideas about the pathogenesis of asthma, and it's opened up new windows of therapeutic treatment," says Freeman, trying to sound reserved as he talks about their unpublished results.

(Translation: We think we know something new about how people get asthma.

All the experiment required was a nonsmoker willing to become a smoker.

If you have any sort of conscience, there's only one person you can ask to do that.

What we know gave us an idea for new drug treatments that seem to work in mice.)

Furthermore, he says, the drugs they are finding success with are cheap, stable, and don't seem to have nasty side effects. They may even be good for you.

Thrilling discoveries like this are rare. They require a lot of hours and a lot of luck. Nevertheless, 6 a.m. Monday will more often than not find Shapiro genuinely pleased to be ascending to the 12th floor of Scaife Hall. He tells medical students that it's easy to get so focused on learning what you need to know to be a great clinician that you never consider working in the lab, but there are major rewards to the research life.

He describes his life as a scientist before taking the job as chair: "If I wanted to go see my kid in the school play in the middle of the day—and I wasn't on service—I could probably work my day around that.

"So you have more control over your life and family issues.

"Also, it's very rewarding after seeing my one-thousandth patient with lung cancer. Boy, you sure want to do something about it—to go back to the bench and change it."
LISTEN TO THE MAN IN Jack Coulehan's poem, wizened and readying to fight. I might not have much body left, he tells the doctors who stand over his bed, but I've got good arms—the polio left me that. Listen to the physician in another poem, his patient stunned by the past. What can you do, he asks, when you're stranded in this hard, brazen country?

What he does, like the narrator in so many of Coulehan's poems, is stand witness. "I have a real belief in, and commitment to, the power of connecting with another person," Coulehan (MD ’69) says. The professor emeritus of preventive medicine at SUNY Stony Brook, and former Pitt professor of family medicine, is the author of four books of poems and a widely used text on the doctor-patient relationship.

For Coulehan, the stories people tell are as important as any objective truth, any scientific fact. The privileging of science is a sign of a "radical misunderstanding" of the nature of healing, he says.

Our view of technology borders on the mythic, says Coulehan, because we welcome the illusion of certainty it provides. The poet who once practiced medicine among the Navajo likens a typical Western patient's relationship to, say, an MRI to a Navajo's relationship to a sand painting. For both, the object is a powerful symbol of healing. "We have a magical belief in science," Coulehan says, "not a scientific belief in science."

Yet, far from dismissing this kind of magical thinking, Coulehan embraces the power of myth to shape human experience. In "Heroes,"
as gunshot victims are rolled into the emergency room, their lavender shirts and bloodied chests eliciting disdain, the narrator suggests:

remember the myth among them—

they are the sons and daughters of dukes, the heirs of dukes, and deserving of love,
they are the lost children of heroes, the bastard progeny of gods

In a poem so much is possible. Here, the physician can set aside, however briefly, the urgency of clinical practice. He can reflect, not only on the lives of his patients but on his own life. Coulehan, who directs Stony Brook’s Institute for Medicine in Contemporary Society, considers such reflection crucial to good doctoring.

Physicians, like poets, live in doubt. They must be able to hold mystery and contradiction in their hands—Keats’ “negative capability.” “At the core of medicine,” Coulehan says, “is a poetic sensibility.”

His latest book, edited with Angela Belli, is Primary Care: More Poems By Physicians (University of Iowa Press, 2006).


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**PHRENOLOGY**

Concavities and lumps above my ear speak narratives I never would have known before relentless loss of all my hair

turned truth about my scalp so baldly clear—the story of my life is in the bone.
Convexities and slumps above my ear

identify the site of passion: here. Like tenacity and hope, it’s in a zone invisible before the loss of hair

writ large the heady script of character. Depression, fancy, awkwardness intone complexity that’s bunched above my ear

for you to read. Your gentle fingers, dear, interpret my desire and mine alone. My scalp is blessed to have no trace of hair.

It shines with gratitude—I love your care for this old scalp, though never have I won a way to read the bumps above your ear, which even now are swathed in silver hair.

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**HANDS**

It’s come to this—bowels. Six weeks from the time you teeter, fall and spend the night strapped to a gurney, your hands lie in wait, jump, grab, tap my fingers. You talk about bowels but hey! Yours are not the hands of misfortune.

They have a life of their own, buds at the end of old boughs. Your skin hangs from sickness, fever, fasting, but not your hands. Your hands put on an old one-two, a little vaudeville between the act in which you lose your brothers, wife and commonsense, and the one where knots are loosened, pipes reamed out and ropes replaced.

Every morning brings a new task, a new way of looking at what’s left. But only your hands leap from the bed. The rest of you is pale, tenuous and devoted to bowels. Just now, when I speak of the future, your eyes water like red springs, but your hands brush my fingers with Hey Bones! and that old soft shoe.
LACHRYMAE RERUN

Fried flounder on cardboard plates, slaw,
drafts of dark beer. Pain has followed us here
to the fish place in Riverhead. I’m fed up
with clammers’ shot backs, bad kidneys,
and their wives’ arthritis. I’m fed up
with cancer wearing suspenders and dousing
its flagrant heart in wine. The tables here
are crammed with pain. The coolers
are stacked with eel like black,
pickled sausage. Go ahead, though, keep talking
about your cancer’s home—the church
you grew up in, its Baroque Italian priest
and pinched nuns that scuttled across your youth
like bugs. You’re not buying it, not an ounce
of original sin, not a word of Augustine,
nor anything that carries you down
from joy. That’s what you say. Even the walls
of this joint are sweating blood, but you’ve
converted to a new belief in the cosmic dance.
Go ahead, keep talking. I’m not thinking now
about the sweating bodies of the dead
in Africa, nor that woman with the bomb
beneath her t-shirt in Sri Lanka, nor the kid
gunned down in Brooklyn, nor the arrogance
of righteous violence. I’m trying to imagine
the original blessing. Go ahead, tell me
the wizened eel of history is somebody’s fault,
Jesus’ or the popes’ and if left to ourselves
we’d surely dance. And be compassionate
and tender. Go ahead, finish your beer.
Let’s kick up our heels. It’s Saturday night
in any case, and I’m tired too, of tears.

ANATOMY LESSON

When I move your body
from its storage drawer,
I brush my knuckles,
Ernest, on your three-days
growth of beard. Cheeks,
wet from formaldehyde,
prickle with cactus.
My eyes burn and blink
as if a wind of sand
blew through the room.

Bless me, Ernest,
for I cut your skin
to learn positions
and connections
of your parts—caves,
canyons, fissures, faults,
all of you. Show me.
Show me your flowers,
your minerals, the oil
of your spleen.

Do not mistake these tears.
These tears are not
for your bad luck
nor my indenture here,
but for all offenses
to your heart—yours, mine—
for the violence
of abomination.
Think of my tears as rain
staining your canyon walls,
filling your stream,
touching the blossoms.
DEPRESSION NEEDN'T ACCOMPANY OLD AGE, SAYS CHARLES REYNOLDS
INTERVIEW BY TERRY GROSS

LOOKING OUT FOR OLD FRIENDS

On September 11, the University of Pittsburgh's Charles Reynolds (Res '80) was featured on National Public Radio's Fresh Air with Terry Gross, produced in Philadelphia by WHYY and distributed by NPR. What follows are excerpts of the interview. (© 2007, WHYY. Printed with permission.)

GROSS: Older people often suffer with undiagnosed and untreated depression. My guest, Dr. Charles Reynolds, says depression should not be regarded as a normal part of aging. Reynolds directs a research center for late-life mood disorders that is funded by the National Institute of Mental Health. It's based at the University of Pittsburgh medical school, where he's a professor of psychiatry, neurology, and neuroscience. Dr. Reynolds, welcome to Fresh Air. You know, there are so many reasons to be depressed if you're very old. There's declining health; that's probably not going to improve. Maybe you've lost a spouse. You've probably lost friends. You're facing more decline as you get older, and you know that that's just going to be followed by death. So you'd maybe say that depression is a natural and even almost sensible state to be in given what you're facing. What would you say to that?
“I’ve known older people who will look at you and say, ‘I’m not crazy. Therefore I don’t need to see a psychiatrist, and I certainly don’t need any medication.’”

**REYNOLDS:** What’s really, I think, surprising, Terry, is how many older people are resilient to clinical depression. Despite the losses that accompany old age... many people don’t in fact develop the symptoms and signs of clinical depression. Rather, they’re able to cope actively with the challenges of old age. Perhaps two in 10 people do, however, become clinically depressed, and it’s important that they be identified and offered appropriate treatment.

**GROSS:** Now, I was once told by a doctor, by an internist, that antidepressants aren’t as effective in the elderly as they are with other people. And that, also, antidepressants won’t be as effective if an older person’s depression seems to be situational—like the loss of a spouse or like facing chronic health problems. Do you think that doctor was correct?

**REYNOLDS:** The data really do suggest otherwise, and let me tell you what I mean. Clinical trials involving the use of antidepressant medications have matured in the last 10 to 20 years. And what we’ve shown, in essence, is that situational depression, such as depression following bereavement, in fact is quite responsive to antidepressant medication and allows the person who is bereaved to be in a better position for doing the work of grief. It removes one of the barriers to doing appropriate grief work and to adjusting to life, say, without the spouse.

**GROSS:** Do you find that a lot of elderly people are resistant to even talking to a psychiatrist? ... I’ve known older people who will look at you and say, “I’m not crazy. Therefore I don’t need to see a psychiatrist, and I certainly don’t need any medication.”

**REYNOLDS:** I do think that is the case. The older generation of Americans, I think, have a very different personal model of what depression is. And we should say that depression doesn’t mean that you’re crazy. It’s a treatable medical illness.

At the same time, I think many older Americans may take the view that depression may somehow represent a moral failing or a character or logic flaw, rather than an illness like diabetes or hypertension, which can be diagnosed and treated...

My own view happens to be that it’s very appropriate for most older Americans living with depression to be treated in the primary care setting. Depression treatment is often a very straightforward medical undertaking. Geriatric mental health specialists like myself can be called in as consultants, or we can offer an opinion on a particularly difficult-to-manage situation.

**GROSS:** When you do talk therapy, as I assume you do with some older patients who you see...

**REYNOLDS:** Correct. Yes. **GROSS:** ... can you give us a sense of what therapy is like—like what topics you’d bring up? ... Especially if somebody is older and their memories aren’t as good as it used to be. Maybe they even have a little bit of dementia. I mean, how does talk therapy work when your mind isn’t what it used to be?

**REYNOLDS:** Talk therapy is actually very helpful for older people with depression. I think it’s important to emphasize that all of these therapies are relatively brief. They’re very active. The patient is not lying on a couch, as you might think of in terms of traditional psychoanalysis. Rather, the patient and the therapist are actively engaged in one form of problem solving or another.

Take interpersonal psychotherapy as an example. Here we’re often dealing with issues related to bereavement, such as the loss of a spouse, or transitions in major social roles, such as can be seen in the wake of retirement.

We might also be dealing with interpersonal conflicts. Let’s suppose an older person with depression is becoming increasingly frail or dependent upon a caregiver, and that relationship has become somewhat conflictual. One of the important focuses of IPT (interpersonal therapy) in a situation like that is to help improve communication with the caregiver in order to lower the amount of tension or stress that’s in that relationship.

**GROSS:** Now, I know while you were doing your residency at the University of Pittsburgh one of your grandparents committed suicide at the age of 89, and I understand that that helped lead you to study geriatric psychiatry. What happened? What do you know about why your grandparent committed suicide?

**REYNOLDS:** Yeah, this was my grandfa- ther, M r. Charlie, as he was called. I’m actually named for him. He was a very successful Mississippi farmer. He raised cotton. He was a— really a great guy, very vital and, as far as I know, had never experienced any depression in his life until he reached very old age. And in his mid- to late-80s, Mr. Charlie suffered a stroke. He also developed a very painful case of herpes, which is common in older people who are frail or whose immune systems are compromised.

And my speculation, Terry, is that in the wake of these medical insults, which were very disabling for him so that he couldn’t really practice farming anymore, I think he came to feel that his life was pointless. He became pessimistic. ... So I think he made the decision that he had no more, in a sense, windmills to tilt at. ... He had a gun in his house and, as is the case with many older men who die by suicide, he shot himself in the head. I found out about that after the fact. And, as your question suggested, it had really a profound impact on me, both as his grandson but also as a budding young psychiatrist at that point. And so for the last really 25 years, this has been the focus of a lot of the scientific and clinical work that I’ve done, and I think we’ve made a lot of progress in trying to prevent the sort of thing that happened to my grandfather.

**GROSS:** Did people in your family feel that if they had intervened in some way that they might have prevented him from killing himself?

**REYNOLDS:** Oh yes, I think this is always, Terry, the emotional legacy of suicide within a family. You always have to ask yourself if it was preventable. And yet the science, I think, tells us two things here that are very important to take note of. A lot of suicide in old age is preventable because it’s the product of depression, which is a treatable illness. My colleagues and I have shown that if you appropriately treat depression in old age, you greatly lower and reduce the amount of suicidal ideation. At the same time, it’s important to remember that mental illnesses, like other illnesses, are sometimes fatal. They can be terminal, and it’s not possible in fact to prevent all cases of suicide, even under the best of circumstances.
And, I mean, people are living in ways that they just never did before. I’m sorry for stammering here, but it’s a very uncomfortable subject to discuss. But there’s just a lot of people who say, “If I get to that point, I don’t want to live that way.”

REYNOLDS: I’m glad that you asked the question, because it’s a conversation that we need to have as a nation—isn’t it?—as well as within our own families and with our primary care physicians. The fastest-growing segment of the population in the U.S. is actually people above the age of 85. That is to say, the frail elderly. It’s very important for all of us to have discussions with family members, caregivers, ministers, physicians, about what our core values and preferences are, about the extent of treatment and support that we want at the end of life. So often we don’t have those conversations. They aren’t reflected in living wills, for example. And yet, if we do have those conversations with significant others and with our physicians, I think the chances are that we’ll have a greater sense of control at the end of life and prevent the kind of scenario that you described.

GROSS: Of course, you know, living wills never say, “I have a gun, and, at a certain point, let me use it.” Do you know what I mean? And without sounding cold, I’m wondering if there was anybody in your family who said about your grandfather after he killed himself, “God bless him. He knew what he wanted. He got to a point where he no longer wanted to live. He had a gun. He made a rational choice, and, you know, who can argue with it? Maybe he knew what his limits were and, by his standards, he did the right thing.”

REYNOLDS: You know, I think that’s a very understandable point of view, and I struggle with that myself. And at times I think, Terry, I’ve comforted myself as a grandson with that point of view. You know, at the same time, though, the science tells us something that may be slightly different from that interpretation. If you provide appropriate clinical management or treatment to [older adults] living with depression or with emotional or spiritual or psychological pain, very often their desire to end their lives may actually go away. And they may decide that it’s worth sticking around for a little bit longer.

GROSS: What advice would you have for people who have an elderly parent or grandparent or spouse who they really feel is depressed and could benefit from psychiatric help, but the person who is depressed doesn’t comprehend that they’re depressed? They refuse to do anything about it, to see anybody about it, and, in fact, even accept it as an insult that somebody would think that they are depressed and that they need help.

REYNOLDS: Your question is so very important because, as you’ve just said, many older people simply don’t, or won’t, recognize clinical depression in themselves.

Also, it’s very difficult to be the family member or caregiver of an older person with depression. Depression is almost like a contagious illness, and many of the caregivers of our depressed patients are themselves suffering from mild forms of depression.

There are some practical things that a family member or caregiver can do. First of all, it may be better not to use the D word, the depression word, which may be so stigmatized for older Americans that it represents an absolute barrier to help-seeking. Instead of depression, they hear “crazy.” So it may actually be better to use terms that are out of the everyday vocabulary or experience of an older depressed person. Perhaps they’re tired day in and day out or not enjoying most of their usual activities. Maybe they’re worried. Maybe they’re not sleeping well. So a family member can talk to the older person in terms of their actual lived experience of depression. Under those circumstances, it’s often possible to persuade an older family member to get help.

Now, the help may be from a trusted professional. Perhaps that is going to be a minister or a priest or a rabbi. Maybe it’s going to be a primary care doc with whom they’ve worked for many years. The impor-
Pitt researchers help out at a camp for those with a rare genetic disorder that hampers the DNA-repair pathway. At Camp Sundown, kids get to stay up all night.
It’s almost 9 o’clock on a warm, humid July evening in the woods in eastern New York State. The sun, as it dips beneath the horizon, sets wispy clouds ablaze with a crimson glow.

At the far side of a large clearing, next to a silent forest, you can just make out the silhouette of a long, low-slung building that looks like a military barracks. No lights can be seen from its windows. It looks uninhabited.

Just 10 minutes later, the sky turns ultramarine and floodlights illuminate the entire exterior of the building. The double doors that bisect the structure burst open. From them pour a couple dozen people who have been living inside in a self-imposed exile from sunlight for the past few days.

This is Camp Sundown, in Craryville, N.Y. The camp brings together a group of children, teenagers, and adults who suffer from xeroderma pigmentosum, or XP, a rare genetic disorder that renders people unable to tolerate ultraviolet light. Because their skin cells cannot repair the damage caused by UV rays, people with XP are thousands of times more likely to develop skin cancers as other people. So, they and their families live for the night.

Camp Sundown is run by Caren Mahar, a 46-year-old mother of five whose 15-year-old daughter, Katie, was diagnosed with the condition as a toddler. Mahar and her husband, Dan Mahar, established the XP Society along with the camp in the mid-1990s. They eventually raised almost a million dollars to build the barracks, which looks more like a dimly lit Holiday Inn on the inside than a military abode.

This year at Camp Sundown are children, teenagers, and adults with a range of symptoms, some mild and some very severe, depending on which genetic mutation they have and where it occurs in the DNA-repair pathway. Niedernhofer notes that there are seven “complementation groups” for this disease, meaning seven different genes can be affected. If the mutation is upstream in the DNA-repair pathway, XPers tend to have milder symptoms. If it is downstream, they tend to have more severe disease.

On this night, the XP campers and their families, who number 41 in all, will travel to the town of Campbell Hall, N.Y., which is about an hour-and-a-half bus ride away. They’ll attend a festival and play baseball against a minor league team.

While the group waits for the bus to arrive, Mahar, who describes herself as “a sliver under five feet tall,” rattles off orders to the almost dozen assembled volunteers with the authority of a drill sergeant:

“Every family has to be escorted at all times no matter what happens. Do you understand?”

Among the volunteers are four members of the laboratory of Laura Niedernhofer, an MD/PhD assistant professor of molecular genetics and biochemistry in the University of Pittsburgh School of Medicine. At Pitt, Niedernhofer studies the molecular and cellular processes involved in aging. Her group and others discovered that DNA damage, when not repaired, promoted aging. Therefore, a defective DNA-repair mechanism in early life can lead to premature aging. People with XP have an accelerated aging process, says Niedernhofer.

Sensitivity to the sun and a dramatically heightened risk of skin cancer are the main features of XP, notes Niedernhofer. “But as more and more of these individuals are being protected from the sun and are living longer, other types of symptoms consistent with premature aging are being discovered,” she adds.

“The most predominant feature is a decline in their motor and mental skills, or neurodegeneration. They also develop problems with their hearing and vision, just like you would see in someone who is in their 70s or 80s. But, in Xpers, these things can begin showing up as early as their 20s and 30s.”

Among the Xpers at Camp Sundown this year are children, teenagers, and adults with a range of symptoms, some mild and some very severe, depending on which genetic mutation they have and where it occurs in the DNA-repair pathway. Niedernhofer notes that there are seven “complementation groups” for this disease, meaning seven different genes can be affected. If the mutation is upstream in the DNA-repair pathway, XPers tend to have milder symptoms. If it is downstream, they tend to have more severe disease.

These families may live in the dark, but they’re illuminating science.

“Much of what we have learned about DNA damage recognition and repair comes from studies on XP patients, like the Camp Sundown campers,” notes Arthur S. Levine, dean of the medical school, senior vice chancellor for the health sciences, and a DNA-repair researcher himself.

Niedernhofer has been bringing members of her laboratory staff to Camp Sundown for the past several years. This year she’s brought seven members of her lab at her own expense. Among them is Siobhan Gregg, one of the laboratory of Laura Niedernhofer, an MD/PhD assistant professor of molecular genetics and biochemistry in the University of Pittsburgh School of Medicine. At Pitt, Niedernhofer studies the molecular and cellular processes involved in aging. Her group and others discovered that DNA damage, when not repaired, promoted aging. Therefore, a defective DNA-repair mechanism in early life can lead to premature aging. People with XP have an accelerated aging process, says Niedernhofer.

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of Niedernhofer’s graduate students who is getting her first exposure to people with XP. Until now she has only worked with XP mice, which Niedernhofer helped to develop.

“It was a bit intimidating when I first arrived,” says Gregg. “But the families and kids really appreciate our being here and make us feel right at home.”

Gregg and her labmates play games with the campers and help out with events. Because the camp includes family members who do not have XP and can be up and around during the day, someone needs to be available around the clock to help out. Niedernhofer and half of her lab took the day shift; she has left the night shift to the other half of her lab group, which includes Gregg.

Earlier in the day, Niedernhofer delivered a short lecture on her research to the families attending the camp. Although there are no currently available treatments for XP other than avoiding the sun, her lab is experimenting on mice with compounds that may be able to alleviate the damage to skin cells caused by UV light.

“What the families really ask for is a bit of hope,” says Niedernhofer. “We are at a very early point in our research for treatments. … But we anticipate that someday we’ll recruit patients from this group for more detailed analyses of the disease in humans and clinical trials.”

The school bus arrives at 9:30 p.m., and campers immediately begin boarding for the long drive. The teenagers migrate toward the back, while the adults with smaller children sit in the middle. Several campers who are in wheelchairs are put in the front. As instructed, Gregg and the other volunteers post themselves throughout the bus. As the bus heads off into the starlit night, some of the teenagers nod in time to music only they can hear through their ear buds. Others tease each other good-naturedly or tell bad jokes evoking a smattering of groans and giggles. Adults sit in silence or make small talk. Some of the younger children begin to doze off.

About 45 minutes into the trip, as the bus is motoring down the interstate, the passengers are startled out of their seats with a kaboom! The bus has a flat, and the driver immediately begins easing the vehicle onto the shoulder of the highway.

Mahar, who has been following in her Hyundai Santa Fe, boards the bus and tells everyone to stay put. Within a couple of minutes, a highway patrol officer pulls up and, after a short consultation, asks the driver if she can make it to a nearby rest area, where it is safer to make repairs. The bus has double tires on the back, so she is able to drive it, albeit with a loud thumping from the flat tire, slowly to the rest area, which is about 5 miles further down the interstate.

It’s after midnight by the time the bus makes it to the rest stop. Mahar makes calls to Campbell Hall organizers, apprising them of the situation. They are still willing to hold the baseball game, but Mahar is growing increasingly doubtful that it can take place.

In between calls, she recounts the story of a nighttime cruise around the Statue of Liberty. On the ride home, the bus driver took a wrong turn and got lost in Manhattan. Because it was starting to get late, campers with the most UV sensitivity were loaded into a van that had been trailing them.

The van was able to get them back before dawn. The rest of the group, however, got back almost an hour later and watched in horror as the sun began to rise. Although everyone arrived safely back at camp, Mahar said it forced her to take more precautions. Now she always follows the bus in another vehicle with specially tinted windows that is large enough to hold several campers. “We are always racing against the sun,” she says.

It is well after 1 a.m. when the repairman arrives to fix the flat tire. By now, Mahar has called off the baseball game because there is not enough time. No one complains. Then Ronald McDonald arrives from the festival with a van full of gifts and refreshments for the kids. The clown lifted spirits, notes Gregg later: “The kids and families went from feeling nervous about the bus situation to enjoying themselves and laughing.”

At almost 2:30, there is no time to waste. The campers get back on the bus. Mahar loads several into her car and goes on ahead. By the time the bus rolls back into camp it is nearly 4:30 a.m. The campers file off the bus and immediately head inside in silence to the safety of their rooms. Within minutes, a glow begins emanating from the eastern sky.

Because their skin cells cannot repair the damage caused by UV rays, people with XP are thousands of times more likely to develop skin cancers as other people. So, they live for the night.
Ake Grenvik is notoriously unflappable, even jumping out of an airplane at 14,000 feet, as he did at age 75 in 2004. He calls the jump, which ended with a soft landing after reaching speeds of 146 mph, "uneventful."

"I was a flight surgeon before coming to the U.S.,” says the critical care expert. (He doesn’t mention that was 40 years ago.)

The field of critical care medicine as a subspecialty began in the University of Pittsburgh School of Medicine in 1962, when the late Distinguished Service Professor Peter Safar founded the first critical care residency program in the United States. In the 45 years since, close to 700 physicians have been trained at Pitt in the art of caring for patients at their most vulnerable—when they are on life support or when they require organ-simulator-aided medical education.

During their time in Pittsburgh, most of those physicians—a vanguard of critical care expertise that is now scattered across the globe in some 50 countries—became intimately familiar with the particular joys of rounding in the intensive care unit at 4 a.m. At least that’s what Grenvik, the stern taskmaster of those predawn rounds, says with a chuckle. Besides Safar, no one person did as much to advance the critical care program in Pittsburgh as Grenvik, who led the training program for 25 years and is now a Pitt Distinguished Service Professor of Critical Care Medicine and professor of anesthesiology, medicine, and surgery. In recognition, the Department of Critical Care Medicine is raising funds to create the Ake and Inger Grenvik Chair, which will be held by a Pitt physician-scientist with extraordinary strengths in critical care research and simulator-aided medical education.

Grenvik received his MD and PhD in his native Sweden, where he trained as a cardiothoracic surgeon. In 1966, he published a study of patients on and off mechanical ventilation in the ICU at Uppsala University. Subsequently he was offered a post in charge of that ICU. This would have required anesthesiology training, which was the standard in Europe for intensive care. Grenvik wanted training specific to critical care, so he accepted an invitation to be both a junior faculty member and one of Safar's fellows at Pitt. He never returned to his promised post in Uppsala.

After one year, Safar put Grenvik in charge of the ICU at Presbyterian University Hospital. Grenvik soon discovered that by 7 o’clock in the morning surgeons would begin arriving in the ICU to check on their critical patients. Heart surgeon Henry Bahnsen, the chair of surgery, was a notorious early riser. And the lean figure of Thomas Starzl was a regular presence at the bedside of his liver transplant recipients. Grenvik says that four in the morning was “the time that I found useful” both for the good of the patients and to have them in optimal condition for the surgeons’ rounds.

Initially set up to train only anesthesiologists, the program expanded under Grenvik and now prepares specialists in medicine, surgery, and pediatrics for board certification in critical care. Knowing that medical professionals, including himself, are not necessarily born unflappable, Grenvik was a proponent of Pitt's Peter M. Winter Institute for Simulation Education and Research, which trained some 3,000 people in 12,000 medical encounters last year. In 2001, Pitt’s critical care program officially came into being as the first fully independent department devoted to critical care in an American medical school.
Early in his career, neuroradiologist Charles Kerber (MD ’62) was shown an image of a little girl with a tangle of abnormal bleeding vessels in her brain. “You think you’re so damn smart with catheters,” said his frustrated colleague, a pediatric brain surgeon preparing to operate. “Why can’t you get up there and fix this?” The tools didn’t exist then. When the little girl died, Kerber went home to his basement workbench and made a tiny flexible catheter with a silicon balloon. Later a woman came into the hospital with the same condition. This time, Kerber was ready. With the husband’s permission, he threaded the microcatheter into an artery and applied an experimental glue-like suture substitute. “She woke up the next day,” he says.

Kerber, a professor of radiology at the University of California, San Diego, now uses MRI to study the way that blood flows in the body. He also flies his own Russian-made military jet. “I got into flying because I was a kid working on a farm, ankle deep in cow manure, and when the first jet flew over, it was wonderful,” he says.

As professor of surgery at the University of California, San Francisco, Nicholas Feduska (MD ’67) was part of one of the most active kidney transplant centers during the 1970s. He completed more than 2,000 successful transplants. In 2005, Feduska decided it was time to shed the white coat. He says he reached a point where continuing to practice became financially foolish. “The cost associated with practicing was progressively increasing, and income from practicing was progressively decreasing.” Since 2006, he’s been a realtor in the Las Vegas area.

Randolph Miller (MD ’76, Internal Medicine Resident ’79) was a second-year med student—a physics major from Princeton University who knew how to program computers—when he volunteered to help Pitt’s Jack Myers with a project in computer-assisted diagnostics. Today, Miller is the Donald A.B. and Mary M. Lindberg University Professor at Vanderbilt University and was recently elected to the Institute of Medicine. “I was recruited here as chair of what became the Department of Biomedical Informatics,” he says, noting he has since stepped down. Now, he’s considering a return to his original work, trying to build a national model for computer-assisted diagnosis.

Mark Hoch (MD ’88), a family medicine practitioner, considers health in terms of mind, body, and spirit. He is an adjunct assistant professor of family medicine/community health at

To make a new ear, Robert Yellon (Fel ’93) harvests rib cartilage from directly below a child’s breast area. He carves the cartilage like an artist creating a sculpture—laying down a general shape, manipulating it with a scalpel, and suturing small pieces of cartilage onto it. The final product is a constructed ear that Yellon, associate professor of otolaryngology and of neuroscience at the University of Pittsburgh, implants on the side of the head of a child born missing an ear.

The implant is stage one of a four-stage procedure completed over the course of one year. In the final stage, if the child’s anatomy permits, Yellon can potentially open the ear canal so the child can hear through it. In the United States, about one child in 6,000 is born lacking an ear. Yellon is one of a few surgeons in the country who specialize in this procedure. He’s also in demand internationally. When he was interviewed for this story, a family in Israel was in touch with him about performing the procedure on their daughter.

As a carver of cartilage, Yellon works in other areas of the body, too.
the University of Minnesota and recently received a Bush Foundation fellowship to pursue a master's degree in theology and spiritual healing. He is past president of the American Holistic Medical Association, which seeks to make holistic medicine a board-certified specialty.

Richard Pan (MD ’91) chairs Healthy Kids, Healthy Future, a five-county collaboration based in Sacramento, Calif., that provides insurance for uninsured children who do not qualify for other public health coverage. He won a 2007 award from Sacramento's Child Abuse Prevention Council for his work. Pan also directs Communities and Physicians Together, which sends University of California, Davis, resident physicians into neighborhoods to partner with organizations that improve health care for families. He is chair of the California Medical Association’s Council on Legislation and an associate professor and associate residency director at UC Davis.

Jair Soares (Psychiatry Resident ’97) was appointed professor of psychiatry and director of the Center of Excellence for Research and Treatment of Bipolar Disorder at the University of North Carolina, Chapel Hill, in March. Soares says the new center will combine clinical care and research.

David Dosa (Internal Medicine/Geriatrics Resident ’03), an assistant professor of medicine at Brown University, participated in a roundtable discussion in August 2006 in Washington, D.C., about how long-term nursing care suffered in New Orleans during the aftermath of Hurricane Katrina. Dosa says the catastrophe magnified existing problems in nursing home systems. In July, he made headlines with his New England Journal of Medicine essay about a cat named Oscar. (See page 40 for more on Oscar.)

Before James Gagermeier (Pulmonary, Allergy, and Critical Care Fellow ’05, Transplant Medicine and Interventional Pulmonology Fellow ’06) came to the University of Pittsburgh to train, he was employed by Indian Health Services as a physician for the 2,000 residents of Prince of Wales Island in Alaska. Gagermeier describes a day that began with him surgically repairing one patient’s facial lacerations inflicted by a wolf/dog hybrid and ended with another’s premature labor, which required her being life-flighted to the mainland. In the middle of all that, he administered chemotherapy.

Now an assistant professor of medicine in the division of pulmonary and critical care at Loyola University Chicago Stritch School of Medicine, Gagermeier helps some of the sickest patients in the hospital weather the ups and downs of lung transplantation. He is currently the medical director of Loyola’s lung transplant program.

—Sarah Evans, Matt Minczeski, and Chuck Staresinic

This spring, at the Airway and Voice Center at Children’s Hospital of Pittsburgh of UPMC, he operated on a 7-year-old Nicaraguan boy who had fallen from a tree, landing on a metal fence. He crushed his trachea. Doctors saved the life of this 7-year-old with an emergency tracheotomy, but the accident left him breathing through a hole in his neck. Normal speech was impossible. For the next two years, he was out of school and at constant risk of infection.

Yellon and colleagues used the boy’s rib cartilage to widen and repair his airway. The boy is now able to breathe normally and has begun to recover his speech. He returned to Nicaragua within a few months.

The doctor finds his work enormously rewarding. But ask him to describe his specialty, and he says that he is simply “a whittler of ribs.” —MM AND CS
THE WAY WE ARE
CLASS OF '58

Y
ears ago, while at his family’s vaca-
tion home in Nemacolin, Pa., Law-
rence Ellis (MD '58) visited
Great Meadows, the site of one of
the first battles between the French and the
British during the French and Indian War.
The historic battleground—site of
George Washington’s only surren-
der—inspired Ellis to learn more
about the general. He now has
an entire library of Washington biog-
raphies, including some written just
five years after Washington’s death.
He’s writing his own biography of
Washington with his son. Ellis,
a Pitt professor of medicine, says
“golf and George Washington are
my two hobbies.”

In between flying from
Indiana to D.C. two to three
times a week as the chair of the
National Science Board, Steven
Beering (MD ’58) occasionally
fits in a round, too. He once teed
off with Arnold Palmer at Palmer’s
Bay Hill course in Florida. On the
18th hole, nicknamed the Devil’s
Bathtub, Beering placed a dirty ball
one ball because a lake surrounds
it. Palmer walked over to
Beering’s tee, snatched the ball
from its resting place, and tossed
it into the water. He placed a
gleaming white ball in its place.

“I don’t know what I was looking at and swing like
I did on 16, and I would get it close to
the pin and birdie the hole,” says Beering.
“And what do you know? I put the ball a few feet from the hole and birdied it!”

Beering, formerly the dean of medicine
at Indiana University and, later, the presi-
dent of Purdue University, is a University
of Pittsburgh trustee.

To make ends meet while he was a
junior med student, Sam Granowitz (MD
’58) moonlighted in various hospitals that
lacked house officers.

“You did things back then you could
ever do today,” says Granowitz. “I covered
the entire ER.”

He later interned at what is now UPMC
Mountaineer under Herbert Frankenstein,
the same doctor who delivered him as a
baby. Granowitz says he stayed on staff at
Mountaineer because it was one of the only
hospitals in the area that welcomed Jewish
doctors into practice. He is the coauthor of
L’Chaim, A History of Mountaineer Hospital of
Pittsburgh.

Charles Copeland (MD ’58) remembers
making extra cash—$75 a month—during
his junior year by collecting urine samples
for an experiment professor of medicine
Abraham Isaac Brody was conducting.
Copeland was selected for the job after
Jack Myers recommended him to Brody.
He says being handpicked by Myers and
Brody was “very important to me in med
school.” Copeland was now director of general
surgery at Mercy Hospital in Pittsburgh.

— Matt Minczeski
— Portraits by Frank Harris

GEORGE BERNIER
JUNE 29, 1934–SEPTEMBER 17, 2007

A
s a young man and budding polit-
ic cartoonist, George Bernier
turned down a scholarship from
the School of the Museum of Fine Arts,
Boston, in order to enroll in Harvard
Medical School.

“He felt that being a cartoonist was too often
about celebrating the failure of others, whereas being
a doctor was the complete opposite,” says his
daughter, Elizabeth Lamont.

After training in hematology and oncology,
Bernier joined the medical faculty of Case Western
Reserve University. He later chaired Dartmouth
Medical School’s Department of Medicine. In 1986
he became dean of the University of Pittsburgh
School of Medicine.

Some say Bernier even “looked like a dean.”

“He had a certain dignity,” says Thomas Detre,
Emeritus Distinguished Senior Vice Chancellor for
Health Sciences. “He radiated warmth.”

Under Bernier’s leadership, Pitt’s curriculum
began to introduce patient care earlier, linking the
first two years of science education with clinical
care. One of his major contributions in Pittsburgh,
says Detre, was “the realization that most everybody
learns better by being in smaller groups.”

Bernier left Pittsburgh in 1995 to become the
dean and vice president of academic affairs in the University
of Texas Medical School.

C.H. WILLIAM RUHE
DECEMBER 1, 1915–APRIL 30, 2007

L
iving in Arizona for the past 22 years
could not knock the Pittsburgh out
of Bill Ruhe (MD ‘40). Ruhe’s wife
has a photo of him from last year that
makes her chuckle; she snapped it when a
Panthers football game was on TV and her
husband emerged from his room wearing
dress Pitt gear.

Ruhe was recruited to teach in the
University of Pittsburgh’s medical school in 1941,
and he remained here until 1960. At various times he
was in charge of admissions, student affairs, and the
curriculum committee. He retired as associate dean
and said he knew every student by name.

Ruhe left Pitt for a position with the American
Medical Association, where he was crucial to the
accreditation of continuing medical education.
At the AMA, he eventually became director of its
medical education division, and retired in 1982
as senior vice president for medical education and
scientific affairs. — CS

IN MEMORIAM

1940s
MORTON L. ARONSON
MD ‘42
JULY 4, 2007
WILLIAM S. KECK
MD ‘43B
JUNE 11, 2007
RICHARD C. LYONS
MD ‘44
JUNE 15, 2007
GEORGE V. HUGHES
MD ‘45
SEPT. 6, 2007

1950s
REX H. NEWTON JR.
MD ‘45
AUG. 13, 2007
DWIGHT C. “PETE”
HANNA
MD ‘46
SEPT. 10, 2007
LEONARD B. MYERS
MD ‘48
JULY 8, 2007
ROBERT HOLMES
MD ‘52
JUNE 27, 2007
JOHN WOODSIDE
MD ‘57
APRIL 21, 2007
CARY L. HAMLIN
MD ‘75
SEPT. 2, 2007

1970s
HANNA L. HAMLIN
MD ‘74
APRIL 22, 2007
SANDRA A. HAMLIN
MD ‘76
APRIL 22, 2007
GARY D. HAMLIN
MD ‘78
APRIL 22, 2007
JAMES S. HAMLIN
MD ‘80
APRIL 22, 2007

— Portraits by Frank Harris
Mike Webster was dead.

Bennet Omalu didn’t even know who Webster was when he made a pot of coffee that Saturday morning in 2002 and turned on the television, but the newscasters explained.

Webster was the kind of football player who made Pittsbughers proud. An offensive lineman, he played one of the sport’s most punishing positions for 15 years. Strong, silent, and stubborn, he didn’t draw attention to himself. He just did his job, which mostly consisted of snapping the football into the hands of quarterback Terry Bradshaw then slamming into defensive players hell-bent on tackling the ball carrier. The Steelers won an unprecedented four Super Bowls with Webster. Now he was dead at age 50.

In a matter of hours after hearing this news, Omalu reported to work as usual at the Allegheny County Coroner’s Office, where he was the attending forensic pathologist and neuropathologist. There on the autopsy table was Webster.

An MD educated in Nigeria, Omalu (Fel ’02) had completed a pathology residency at Columbia University, then come to the University of Pittsburgh for two successive fellowships, one in forensic pathology and another in neuropathology. He also received a master’s degree in epidemiology from Pitt.

All morning, the way people talked about Webster on the news had bothered him. Webster’s doctors had attributed some of his health problems to recurrent head trauma he suffered as a football player, yet people described him as an athlete who couldn’t handle life after football. (Webster suffered from depression and dementia, rambled incoherently in his Hall of Fame acceptance speech, made bad investments, became homeless for a time, and hocked his Super Bowl rings.)

Omalu looked at Webster’s brain, which appeared normal. In a typical autopsy, this naked-eye view would be the extent of the brain examination. Omalu went further. He fixed the brain in formalin and took it to labs of his Pitt mentors Steven DeKosky, professor of neurology, and Ronald Hamilton, professor of pathology.

In the brains of deceased athletes, Omalu discovered injuries invisible to the naked eye.

“I subjected it to highly sophisticated immunohistochemical staining,” says Omalu. “A large battery of stains.”

Omalu found large accumulations of an abnormal toxic protein called Tau in the intracellular spaces of Webster’s brain. This is a sign of chronic traumatic encephalopathy—long known to afflict boxers and sometimes referred to as dementia pugilistica.

Since studying Webster’s brain, Omalu, who is now the chief medical examiner of San Joaquin County, Calif., has examined the brains of other professional football players who came to tragic ends. Two committed suicide. Another died in a violent and fiery car crash as he fled police after apparently suffering a nervous breakdown. The brains of all of these men showed similar injuries.

Omalu’s work has attracted critics, who say that he hasn’t examined enough brains to draw conclusions about whether blows to the head suffered in sports created the injuries. He is attempting to examine more brains, but that has proven difficult.

An epidemiological study this year from the University of North Carolina found that a history of recurrent, sports-related concussions in retired football players was linked to increased risk of clinical depression.

In the summer of 2007, a professional wrestler named Chris Benoit apparently murdered his son and his wife, then hanged himself. A few days later, Omalu, having obtained permission from the wrestler’s father, Mike Benoit, flew to Atlanta to retrieve his brain. He fixed the brain in formalin and—because he didn’t want to declare to airline officials what he was transporting—drove 13 hours to Pittsburgh.

Benoit’s brain showed a large amount of protein tangles in the regions of the brain responsible for controlling emotions. Parts charged with sheparding neurotransmitters like serotonin, noradrenalin, and acetylcholine were all damaged, helping to explain Benoit’s major depression and psychotic episodes, says Omalu. Because of the family’s privacy concerns, Omalu did not release his results to the press until September 2007.

“This is not about football,” says Omalu, though his work has brought a great deal of attention to this aspect of the sport. “This is about concussive brain injury in contact sports. All types of sports.”

This year, the National Football League (NFL) instituted baseline neuropsychological testing of all players. (The ImPact test, used by 30 of 32 NFL teams, was developed by Pitt physicians.)

Omalu would like to see the league support research toward a pathognomonic test—one that indicates tissue damage directly and unambiguously. A good example of the sort of test he envisions is Rachel Berger’s. That Pitt assistant professor of pediatrics has developed blood tests that detect tiny amounts of certain proteins in the blood that may indicate head trauma in infants.

Before the beginning of the 2007 season, the NFL started a fund for retired players suffering from dementia. At its inception, a handful of former players applied for disability payments. In a few months, more than 100 had applied, with more than 50 approved.
He’s the cat you don’t want snuggling up to you in bed. On the third floor of Steere House Nursing and Rehabilitation Center in Providence, R.I., an olive brown-and-white feline named Oscar patrols the advanced dementia unit. Oscar is aloof. He is likely to hiss at a Steere resident—unless he somehow senses death is near. Then he’s purring loudly on the bed beside the unconscious patient during the final hours.

His ability inspired geriatrician and assistant professor of medicine at Brown University David Dosa (Res ’03) to write about Oscar for the July 26 issue of the New England Journal of Medicine. Oscar has predicted the deaths of more than 25 Steere residents, and his accuracy has prompted staff to summon family members when he settles in with a patient. He likes to stay on the bed for the final goodbyes. If forced out of the room, he will pace outside the door and yowl unhappily.

A plaque dedicated to Oscar for his “compassionate hospice care” hangs on a wall at Steere House, where he passes it daily on his rounds.
WINTER ACADEMY
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Naples, Fla.
For information
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Pat Carver
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cpat@pitt.edu
www.winteracademy.pitt.edu

FISHER LECTURE
FEBRUARY 27, 2008
3:30 p.m.
Lecture Room 6, Scaife Hall
James F. Holland, MD, Speaker
For information:
www.surgery.upmc.edu

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STARZL LECTURE
APRIL 2, 2008
4 p.m.
Lecture Room 6, Scaife Hall
Herman Waldmann, PhD, Speaker
For information:
www.surgery.upmc.edu

MEDICAL ALUMNI WEEKEND
MAY 16–18, 2008
Reunion Classes:
1948  1953
1958  1963
1968  1973
1978  1983
1988  1993
1998  2003
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medalum@medschool.pitt.edu

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

Time to warm up for Medical Alumni Weekend 2008. Dust off your copy of the Hippocratean—as we did here with the 1963 edition—and reminisce. Extra credit for anyone who can tell us a good med school story about these or any other members of the Class of ’63. Send your stories to medmag@pitt.edu, or 400 Craig Hall, Pittsburgh, PA 15260.

Medical Alumni Weekend
May 16–18, 2008

For a list of classes having reunions this spring, turn to the other side of this page.

FOR MORE INFORMATION: 1-877-MED-ALUM
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PHOTOGRAPHY: HIPPOCRATEAN, 1963