PITT MED

PITT SURGEONS TRACK

AN INVISIBLE SUSPECT
Pitt Med has expanded its circulation. We now count physicians who completed their residencies and fellowships through University affiliated hospitals among our readers. Welcome all.

During that wild blur known as your training, some interesting things must have taken place. If you have memories to share or other story ideas, we would like to hear them. And boy are we itching to learn what you've been up to all these years. Our bet is your old friends are as well.

Drop us a line via E-mail, fax, or the Pony Express (see contact information below) or fill out the Class Notes form in the back. We're always looking for good fodder.

UNTANGLED WEB
For a look at the magazine's new web site—
http://www.health.pitt.edu/pittmed

We gladly receive letters and whatever else you would like to share. (We may edit letters for length and clarity.)
Pitt Med, 400 Craig Hall, University of Pittsburgh, Pittsburgh, PA 15260
Fax: 412-624-1021; E-mail: medmag@pitt.edu

YOU REMEMBERED!
Make someone's day. Surprise your old colleagues with a story or photo that will take them back. At Pitt Med, we're scouting for those special somethings to enliven our “Footnote,” “Flashback,” and “Last Call” sections. Maybe something funny, maybe something sad, maybe something intriguing. Even if we can't find a place for your idea, we'll make it worth your while: You guessed it; you'll get on our “Free Lifetime Subscription” list.
Sometimes, modern medicine’s miracles are not enough. The old Falk Library ain’t what it used to be. Like mother, like—don’t say it!

Resusciti Anne has a little brother. Julie DeLoia thinks the uterine lining may affect fertility in ways we don’t understand. This just in: Schizophrenia alters basic nervous system circuitry.

Da, these folks are generous.

Ewwww—that’s cool! Paul Caplan goes beyond the back twinge.

When the new chair of family medicine was born, her mother wasn’t allowed to deliver in the local hospital.

Legends in their own time?

It’s invisible, has a half-life of six seconds, and disappears when its work is done. Scientists are just starting to understand nitric oxide’s physiological importance, and Pitt surgeons have led the way.

If the Area of Concentration program is extra work, students haven’t noticed.

Richard Simmons wants to put surgeons like himself out of business.

Get him a cocktail napkin: It looks like Robert Bridges has served up a promising treatment for cystic fibrosis.

He’s considered a father of modern mammography, but Robert Egan, MD ’50, claimed America’s peculiar attitudes hampered advancements.
We need to develop sufficient rapport with our patients so that they are comfortable discussing their concerns, hopes, options, and choices. Our patients should feel well cared for and able to discuss openly, without embarrassment, any experimentation with alternative therapies. Further, our medical students must be well informed about the conceptual basis, safety, and efficacy of alternative therapies, the power of the placebo effect, and the psychodynamics of the doctor-patient relation. None of this can be relegated to an elective. Rather, what I have discussed must be incorporated into the required curriculum of our school. Our patients should feel well cared for and able to discuss openly, without embarrassment, any experimentation with alternative therapies.

And so-called cures are out there, everything from coffee enemas to acupuncture to herbal concoctions. This is big business. Each year, Americans make more than 600 million visits to complementary and alternative medicine (CAM) practitioners, which is 200 million visits more than they make to their primary care physicians. The price tag for CAM treatments and services is an estimated $27 billion yearly.

CAM has become hugely popular for a number of reasons: a widespread view that modern medicine is excessively technocratic, bureaucratic, and impersonal; the antiscientific attitudes of new-age mysticism; vigorous marketing; the belief that “natural” remedies are necessarily safe and gentle; and wishful thinking. Moreover, therapists and patients might conclude that an ineffective therapy works if the disease being treated has run its natural course (independent of any treatment), if the disease is cyclic, if it is characterized by not-infrequent spontaneous remission, or if the disease was misdiagnosed initially. The most important reason for a doubtful remedy being credited with an improvement is the ubiquitous placebo effect. One of the fundamental advances in medical science has been the recognition of the power of the placebo, with more than 30 percent of patients visiting a physician deriving benefit from the placebo effect—whatever the illness or its conventional treatment. However, many patients believe that physicians ignore the interaction between mind and body—clearly not the case, as reflected in any medical school’s curriculum.

Another important advance in medical science has been the development of sophisticated methods for the design and interpretation of controlled clinical trials. Thus, modern conventional medicine is based on evidence, and alternative therapies are based on beliefs.

The medical profession cannot put its head in the sand and hope that alternative medicine will go away. The only way to debunk a bogus treatment—or validate a promising therapy—is to test it in a controlled clinical trial. In addition, we need to be well informed about the safety of alternative therapies. Many valuable medications have been derived from herbs and botanicals, yet people treated with the herb aristolochia fangchi have developed renal failure, and St. John’s Wort increases the rate of metabolic degradation of many medications (such as the HIV protease inhibitors).

We need to develop sufficient rapport with our patients so that they are comfortable discussing their concerns, hopes, options, and choices. Our patients should feel well cared for and able to discuss openly, without embarrassment, any experimentation with alternative therapies. Further, our medical students must be well informed about the conceptual basis, safety, and efficacy of alternative therapies, the power of the placebo effect, and the psychodynamics of the doctor-patient relation. None of this can be relegated to an elective. Rather, what I have discussed here must be incorporated into the required curriculum of our school. Our patients are speaking to us through those 600 million CAM visits. We must do more than look at our watches.

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

The rigors of med school are no barrier to Opeolu Adeoye's (MD '02) involvement in issues he cares about. Last year, the third-year student cooked meals at a homeless shelter with African-American male teenagers—as part of a mentoring program he cofounded at Westinghouse High School in Pittsburgh. He also cofounded Life Issues for Education at the University of Pittsburgh School of Medicine, which examines issues of palliative and hospice care. The Association of American Medical Colleges has recognized Adeoye's concern for justice in medical education and health care, awarding him the Herbert W. Nickens Scholarship. He was one of five students nationwide to receive the $5,000 award. Despite his wide-ranging involvement, don't expect to pick up time-management tips from Adeoye. “I must have managed my time well somehow,” he says. “It never felt like it.” —DH

AFTER THE GOLD

How do you follow winning a gold medal, like the one Savio L-Y. Woo received when he won the 1998 Olympic Prize for Sports Science? For Woo, director of Pitt's Musculoskeletal Research Center, the medal was just his first round of Olympian honors. He was recently appointed the first general secretary of the International Olympic Committee’s new Academy on Sports Science, which is made up of 28 physicians and scientists. The elite academy sponsors symposia and research to help everybody who participates in sports, not just the Jesse Owenses among us. Its guiding philosophy, not surprisingly, meshes with Woo's. He sees the games as a way to inspire all of us to improve our health through physical activity. —DH

FOOTNOTE

For this next trick, he'll need a plant. “A volunteer from the audience?” asked Brad Sobolewski, MD '04, ready to perform his act, Interpretive Hair Styling, during a med school talent show. A brave soul stepped onto the stage. Sobolewski took a few fake snips near his head, then flourished a razor. Tresses fell, and fell, yet the “volunteer” smiled. Soon, not a hair was left.

Devoted to noteworthy happenings at the medical school...
Faculty Snapshots

In Japan and other countries adopting a more Western lifestyle, the incidence of diabetes is on the rise, says Linda Siminerio, assistant professor of medicine, who was recently appointed vice president of the International Diabetes Federation. “The rates of obesity are increasing, and with obesity you get diabetes,” she says. Siminerio plans to enhance awareness of diabetes globally. “Diabetes care is poor throughout the world, so we need to do a lot of patient and provider education, too,” she says.

Women are more likely than men to report more disability after a traumatic brain injury, according to a study by Amy Wagner, instructor of physical medicine and rehabilitation. “We found that 70 percent of males consider themselves to be fully employable following the injury, while only 22 percent of women consider themselves fully employable,” says Wagner. She plans further studies to determine why.

Herceptin, a new drug used to treat metastatic breast cancer, is cardiotoxic, warns Arthur Feldman, professor of medicine, in a recent Circulation editorial. The editorial draws attention to statistics presented at the Food and Drug Administration hearings on Herceptin, including the following: 28 percent of women who received the combination therapy of Herceptin and Adriamycin developed heart failure. “Our major concern is that there are studies planned or about to start where they’re going to use Herceptin in women with much less severe disease,” he says. “We wanted to raise a flag of caution.” —DH

Miracles Aren’t Enough, So RAND and Pitt Partner

“Even today—when modern medicine offers an inexhaustible source of new miracles that create, prolong, and restore life—many people in our region fail to receive the most basic health care services,” Harold Pincus, director of the new RAND-University of Pittsburgh Health Institute, wrote recently. The institute plans to use western Pennsylvania as a testing ground for some of the most promising care-intervention strategies; it already has launched collaborations focusing on concerns such as breast cancer and perinatal mortality.

Pincus, who also serves as vice chair of psychiatry for the school, gives an example of how the institute might approach an issue of special interest to him. “In depression,” he says, “there’s an enormous array of research documenting effectiveness of medications and psychotherapy; and there are different care models for applying those treatments.” Yet, he notes that even those who conduct such research have trouble implementing their findings. “There are barriers at each level of delivery,” he says. Pincus likes to break down those levels into “the six Ps”—patient, provider, practice, plan, purchaser, and population: He explains that with depression, the disorder tends to make people think they are not worthy of treatment. Then, even if patients come in the door, providers might not be effective if they don’t approach the disorder as a chronic problem. Potential glitches continue at the population level—in Pittsburgh, for example, one needs to take into account the special needs of the elderly.

All those Ps spell a hopeful prognosis for the region’s health. —EL

Flashback

It was more than 40 years ago, but Bob Badwey’s (MD ’59) friends remember it as though it were the first game of the XFL. A neighbor played the trumpet, and that drove Badwey nuts: There was no way he could study with all that noise. One day, he announced he would put an end to it and stormed out. It wasn’t long before he came back looking sheepish. Turns out, Joe Walton—who weighed in at 215 pounds as an All-American end for the Panthers—was a pretty good horn player.
BOYER LENDS HIS GENIUS TO PITT

Ever since Herbert Boyer and Stanley Cohen started thinking, *Hey, maybe we could replicate DNA if we just snipped it out of the nucleus and... things haven’t been the same.* By inventing gene-splicing, or recombinant DNA technology, they changed the parameters of potential treatments for innumerable disorders and gave rise to the biotechnology industry. Boyer, a founder of Genentech, in South San Francisco, California, has accepted an appointment to Pitt’s Board of Trustees, which can only be fortuitous for the University’s attempts to establish Pittsburgh as a biotech hub. With his wife, he also recently endowed a chair in molecular biology in the Department of Biological Sciences.

(Did we mention that Boyer is a Pitt PhD grad? Arts and Sciences ’63.) —EL

A BIG BOOST FOR GENE THERAPY

There are stamps of approval, then there are stamps of approval.

The National Heart, Lung and Blood Institute (NHLBI) has awarded the School of Medicine $14.3 million to establish the Cardiovascular Gene Therapy Center, which will explore the therapy’s promise for treating cardiovascular disease, the number one cause of death in the United States. The grant will allow clinicians and scientists to train in the latest technologies and procedures. To top that off, the NHLBI has identified Pitt as the national source for producing the vectors, or gene-transport systems, to be used in clinical studies it funds. The grant’s principal investigators include department chairs Joseph Glorioso (molecular genetics and biochemistry) and Timothy Billiar (surgery). Among the many faculty funded by the grant is Edith Tzeng, of surgery; to learn how she is using gene therapy to stop blood vessel walls from narrowing, see page 17. —DH

@Home or Away: Falk Library

BY MARK JACOBS

Sunday morning at home, a physician pours a cup of coffee. It’s time to get her hands on that article in *JAMA* in preparation for tomorrow’s meeting. Gone are the days of braving the rain for a trip to the library. She goes online to the University of Pittsburgh Health Sciences Library System (HSLS) web page. Through her affiliation with Pitt, she is able to search for the article and print it out. All at home, all before the coffee gets cold. And home can be anywhere in the world.

The number of online journals has accelerated from a standstill of zero three years ago to 1,500, says Patricia Mickelson, HSLS director. Library patrons also have access to 80 online and searchable textbooks; these books never get stale because the latest editions are always available.

There’s more whiz and sparkle in digital transmission, yet the library is doing what it always has, notes Barbara Epstein, HSLS associate director: “But doing it with different containers and different technology.”

FOR MORE INFORMATION: http://www.hsls.pitt.edu
A n anonymous grateful patient has endowed a chair in recognition of Lawrence Ellis, MD ’58, professor of hematology/oncology. Ellis’s work on the diagnostic value and methodology of bone marrow biopsy is cited in probably every hematology textbook. He has personally performed more than 7,000 bone marrow biopsies. Donald Trump is the first to hold the chair. He is chief of the division of hematology/oncology and deputy director for clinical investigations at the University of Pittsburgh Cancer Institute (UPCI). Trump’s research focuses on new therapies for prostate cancer. “We’ve developed substantial evidence that administration of very high doses of vitamin D is safe and provides distinct antitumor effects in laboratory models as well as in patients with advanced androgen-independent prostate cancer,” says Trump.

As the new chair of the Department of Dermatology, Louis D. Falo Jr. (an MD/PhD) hopes to interweave more closely its clinical and research programs, so that they optimally contribute to each other as well as the department’s educational mission. His own research focuses on designing new vaccines that are injected into the skin to fight against melanoma and viruses such as human immunodeficiency and human papilloma.

Cells have a built-in defense against cancer—their ability to repair damaged DNA. The February 16 landmark issue of Science, devoted to the human genome, includes an article coauthored by Richard Wood, the Richard Cyert Professor of Molecular Oncology, describing the 130 known human DNA repair genes. Also in the issue is Craig Venter et al.’s analysis of the sequence of the genome. Wood came to Pitt in March to lead the molecular and cellular oncology program at UPCI. He will recruit other scientists to join the program, to be housed, eventually, in the new Hillman Cancer Center. —DH

THE STRENGTH OF NUMBERS
Huge research programs such as the Human Genome Project generate huge continents of data. That’s called for some serious number crunching, since new methods must be found to organize and interpret the results. Recognizing computation is now an essential tool for modern biology, the School of Medicine has created the new Center for Computational Biology and Bioinformatics. Computational biology simulates biological processes through three-dimensional modeling, and bioinformatics is the science of organizing and analyzing enormous quantities of biomedical data.

Ivet Bahar, newly arrived from Istanbul, Turkey, will direct the center. Formerly director of the Polymer Research Center in Istanbul and a visiting scientist at the National Cancer Institute, Bahar has been conducting research at the intersection of computational and structural biology (which studies the three-dimensional structures of large molecules, such as proteins, and their interactions). —MJ

Appointments

T E X T  M A R K E R

O F  N O T E

P I T T M E D
ALUMNI CHECKUP WITH MARIAN MARQUIS AND AMY SAGE

LIKE MOTHER, LIKE—DON’T SAY IT!

BY DOTTIE HORN

SURE, IT WAS CAUSE FOR CELEBRATION—THE GRADUATION CEREMONY WHERE SHE WAS TO RECEIVE HER MD FROM PITT. STILL, AMY SAGE, MD ’99, was a little nervous. As she waited her turn to walk across the stage at Carnegie Music Hall, she thought back to her first week of medical school, when she’d walked across another stage, during the White Coat Ceremony. As a roomful of new classmates watched her don the garb of a physician for the first time, the speaker announced: Amy’s mother just graduated from Pitt’s medical school! Nearly four years later, she had a touch of anxiety. As she reached for her diploma, she wondered, would they make an announcement about her mother? A few people even mistook her for her mother: Marian, didn’t you graduate? It became a running joke with her friends and her mom. “It seemed like everyone loved her,” Sage recalls. That made Sage proud, yet at times, especially before she had carved out her own place at the school, she wanted to say, “Enough about my mother. Let’s just talk about me.”

There was a time when the idea of anyone in the family going to medical school felt like a dream. One of 13 children, Marquis married her high-school sweetheart when they were both 18. Her husband started college at Pitt; then Sage was born. “I worked as a domestic,” says Marquis, “taking Amy with me, cleaning and doing laundry for other people to make ends meet. At that time, we wondered if we would ever stop struggling.” When her youngest daughter started kindergarten, Marquis started on her undergraduate degree at Pitt and eventually entered medical school, at the age of 37. Now, she can hardly believe that her family’s days of scraping by are over. “Every day, we think, ‘Wow, could this really be happening?’” she says.

In the end, sharing the same profession has brought mother and daughter closer, Sage says. “I’m able to say, ‘Gosh, Mom, I was in the ER the other night, and they said that we should do it this way.’ She’ll say, ‘Well, I just read an article and we’re starting to do it this way.’ That is just incredibly wonderful to have that exchange with her,” says Sage. “It’s amazing to be able to do that with your mother.”

FOOTNOTE
You’re doing something right when the admissions director at your alma mater is a happy patient. Pitt’s director, Linda Berardi-Demo, had been feeling queasy when her internist, Mike Finikiotis, MD ’89, called to follow up with her from his daughter’s soccer game. Today, as she screens applicants, she wonders, Another Mike Finikiotis? He has become her “gold standard.”
A healthy woman in her mid-20s shouldn't die on the operating table from an appendectomy. Instead—through anesthesia—she should have a pain-free operation and awaken hours later.

First, the anesthetic should kick in, causing her to fall into a deep sleep. This state, as expected, would stop her breathing, so a tube would have to be inserted through her mouth, past the vocal chords, and into her lungs. Machinery would then breathe for her throughout the operation. That should happen.
There was no reason to anticipate any deviations during this young woman’s appendectomy. But after she was sedated, there was a problem. Swollen tonsil tissue, which was undetectable during the preoperative examination, prevented insertion of the tube—she was suffocating. Every passing minute presented a greater risk for brain damage. After 10 minutes, she would be dead. With the heart monitor beeping ever more slowly in the operating room, the anesthesiologists resorted to rarely practiced invasive techniques. The steady drone of the heart monitor chronicled the ending to this sad episode.

That patient’s medical emergency—unanticipated difficult airway management—occurs once in every 2,000 operations. As an assistant professor and director of the University of Pittsburgh School of Medicine’s simulation center for the anesthesiology/critical care medicine department, John J. Schaefer III provides training to prevent these fatalities, a tricky job: “If I have to open a hole in your throat, how do I go practice that?” he asks.

Before 1990 there was no straightforward way. But in the early 1990s, a simulator for airway management, costing around $250,000, became available. Schaefer’s enthusiasm for the teaching tool turned to frustration. He found it complicated to run. That made it difficult to create clinical scenarios similar to the appendectomy patient’s plight or more frequent airway problems caused by conditions such as cancer or obesity. Not helping matters was the price tag. “I was stuck on one part of it, how to make the vocal chords close.” None of the materials he tried generated an accurate portrayal of the vocal chords closing. He didn’t know what to do. The answer lay at his feet. “I saw one of my kid’s toys—these [oversized plastic] keys—lying on the floor, and I grabbed them and used [the ring] section of the keys to actually fix the last thing.”

A prototype was born, complete with real-life effects such as tongue and throat swellings, a stiff neck, and changing respiratory rates. “I recreated the anatomy of the airway,” he says proudly. His toy-store effects were more lifelike and easier to program than the pricey simulators.

With his “sounding board” and collaborator, René Gonzales, Schaefer secured a patent in less than a year on the cost-effective design and parts of “AirMan.” Next, the physicians partnered with Laerdal, Inc., which manufactures Resusci Anne, the widely used CPR simulator.

Two years of AirMan testing recently concluded at facilities throughout the world. Schaefer liked the results. In recreating the tragic circumstances of the appendectomy patient, he has seen first-year anesthesia residents take steps that would have saved her. Experts believe AirMan holds enormous promise for addressing training issues related to medical mistakes and could improve the fate of thousands of patients each year.

AirMan is now on the market for about $10,000. The University, in part through Laerdal grant money, will buy three AirMan models and eight “SimMan” simulators, which combine the features of AirMan; a more sophisticated model of Resusci Anne, called Recording Anne; and a full cardiac simulator.

AirMan sales may someday pay for his children’s college tuition, yet Schaefer is more excited that he has developed an effective teaching tool: “It will allow other people to learn well, and that should save lives.”

---

**FERTILE PREPARATIONS**

**IMMUNE CELLS IN THE UTERUS**

**BY DOTTIE HORN**

For 14 days a month, the uterus is busy—anticipating an arrival. Once the uterus is almost ready, its guest, a fertilized egg heading toward it, grows into a cluster of cells called a blastocyst. The uterus’s final preparations ensure that when the blastocyst arrives, it finds a nourishing environment...
in which to grow into a fetus.

Sometimes, however, this normal reproductive process goes awry. Julie DeLoia, assistant professor of obstetrics/gynecology and reproductive sciences, postulates a scenario. Say the blastocyst arrives at the right moment, but the uterus isn’t ready because of some malfunction, so the blastocyst cannot implant itself into the built-up uterine lining, or it implants but then withers away. Could the inability of the uterus to make the necessary preparations be a cause of infertility? Up to 20 percent of infertile couples are diagnosed with female infertility for which no explanation can be found. Hoping to find answers, DeLoia is trying to decipher the steps involved in creating a receptive uterus.

Some of the preparatory steps are already known, in general terms. The endometrium lining the uterus puts out a signal that brings immune cells, known as leukocytes, to the uterus from elsewhere in the body. As the endometrium prepares, it steadily increases its number of leukocytes. They reach their highest point during the one-and-a-half to two-day period when the uterus is ready for the blastocyst. During this receptive phase, 25 to 30 percent of all the cells in the endometrium are leukocytes—at other points in the cycle, they make up as little as 10 percent of endometrial cells.

Why does the uterus beef up its supply of immune cells? The answer may involve the placenta, which starts to grow as soon as the blastocyst implants. “The placenta is like a cancer. It chews up the lining of the endometrium; it chews away the blood vessel so that it’s bathed in blood,” says DeLoia. The leukocytes may keep the placenta from invading too far into the endometrium.

As part of its preparations, the uterus subdues the endometrial immune cells. The blastocyst, which inherits half of its genetic material from the father, would be attacked and rejected by the leukocytes—if it were anywhere in the woman’s body but the uterus. “If you transplant a kid’s skin to his mother’s skin, that would be rejected quite quickly and vigorously; so it’s a unique situation in the uterus,” says DeLoia. On the other hand, the immune cells must be active enough to respond to bacteria and other pathogens that might enter the uterus through the reproductive tract.

DeLoia’s research suggests that in infertile women this normal process of recruiting and subduing the immune cells is out of kilter.

One study showed that the immune cells of infertile women were present in different quantities and acted in different ways than in fertile women. DeLoia is now asking a series of questions to pinpoint more precisely what must happen—leukocyte-wise—to get the endometrium ready. Among her questions: By what signals are the leukocytes recruited to the uterus? How are they subdued once they arrive? She suspects that estrogen—the hormone that is released by the ovary and controls much of female reproduction—plays a role. Immune cells, however, do not respond to estrogen, so DeLoia believes intermediary agents are at play.

She is trying to identify these intermediaries. She approached her search by taking biopsies from the endometria of fertile women when the uterus was receptive to the blastocyst. She removed all the immune cells and treated the remaining tissue with estrogen. The tissue gave off several signaling compounds that act upon immune cells. DeLoia now wonders if the cells that normally make these signaling compounds are somehow impaired in infertile women.

Ultimately, DeLoia hopes to provide new treatment options for women who have unexplained infertility. Her work might also someday help women who don’t want to become pregnant. She hopes to develop a new form of contraception that works by turning the endometrium into an environment hostile to the blastocyst. However, those are long-term goals; for now, there are many more experiments to conduct. “We’re chipping away at it,” she says. “Solved and science aren’t words that go together.”
SCHIZOPHRENIA UNLOCKED

DNA CHIPS TAG CULPRIT GENES

BY ERICA LLOYD

This woman has hugged her only daughter once. That was when her daughter was 63 years old.

Her life is a string of paradoxes. She’s kind and generous, would do anything to help another. You needn’t even ask. Yet she trusts few and is sure that others disdain her—probably, they are plotting against her. Her sense of humor delights with its irreverence, though when she is not telling jokes, she’s likely to be whispering about the “theys” who run things. Usually, she is nervous. Often, she is terrified.

What’s happening inside her mind is an infuriating mystery to her family. It’s a mystery to doctors as well. The precise cause of her disorder, schizophrenia, is up for grabs. Doctors define it by symptoms, which they place in functional categories. Impaired motivation and decreased emotional expression—such as reluctance to embrace a loved one—are classified as “negative” symptoms. Delusions, hallucinations, and thought disorganization they consider “positive.” Disturbances in certain types of memory and intellectual function are the “cognitive” symptoms. A team of University of Pittsburgh faculty members believes it has identified the genes related to schizophrenia’s cognitive symptoms. Pat Levitt, chair of neuropsychology, credits the team’s success to interdisciplinary collaboration and DNA microarray technology. It is clear, however, that the team would not have gotten far had they listened to the naysayers.

For the most part, scientists have studied genes one at a time. Then DNA microarrays came on the scene. The technology and its variants are commonly referred to as DNA chips or gene chips (the latter a trademarked name). By color-coding the binding of chemical base pairs, these little wonders offered the possibility of monitoring the expression of thousands of genes at once.

Applying the technology to an organ like the liver, which has only a few cell types, seemed to make a lot of sense. But using a DNA chip on brain tissue, which is composed of probably hundreds of kinds of cells—that seemed overly ambitious. Levitt and colleagues saw things differently. They thought the technology offered an efficient and industrial approach to studying a complex problem. It appears they were right. Moreover, they had the breadth of expertise to pull off the enterprise. Primary collaborators included Levitt (a PhD molecular and neurodevelopmental biologist), David Lewis (MD psychiatrist and systems neuroscientist), who provided neuroanatomical models, and Karoly Mirnics (MD neurophysiologist and computer scientist), who figured out how to structure the analysis.

People with schizophrenia experience it differently, notes Levitt. “Some hallucinate often. Some don’t seem to have this problem, but can’t plan. Some can plan, but can’t remember,” he explains. To make sense of what was assumed to be a disorder involving multiple genes, the Pitt team focused on the prefrontal cortex, a brain region that affects emotions and memory and has been implicated in schizophrenia. They divided genes into 250 functional gene groups, analyzing 8,000 to 10,000 genes on each chip. They saw differences in gene expression compared to controls in only five of the 250 groups.

“People thought that the data would be highly variable, but most genes hadn’t changed,” says Levitt. After hundreds of hours spent in Levitt’s office teasing apart data sets, the researchers saw a common thread—there was something unusual about how subjects with schizophrenia encoded proteins that come together in nerve terminals to regulate synapse transmission. These findings were not restricted to any one neurotransmitter, such as dopamine. Instead, they showed that the basic circuitry defining how information moves through the nervous system is different in those with schizophrenia.

Most notably, these patients tend to underexpress a gene called RGS4, which controls the “volume” of synaptic transmissions. The RGS4 gene helps our bodies suppress the duration of a signal telling us to experience emotions such as fear. Its decrease on the microarray showed that the researchers saw a common thread—there was something unusual about how subjects with schizophrenia encoded proteins that come together in nerve terminals to regulate synapse transmission. These findings were not restricted to any one neurotransmitter, such as dopamine. Instead, they showed that the basic circuitry defining how information moves through the nervous system is different in those with schizophrenia.

Most notably, these patients tend to underexpress a gene called RGS4, which controls the “volume” of synaptic transmissions. The RGS4 gene helps our bodies suppress the duration of a signal telling us to experience emotions such as fear. Its decrease on the DNA chips can be interpreted a couple of ways: Either RGS4 is not doing its job in schizophrenia, or it is responding to some other dysfunction. Regardless, RGS4 deserves the attention of scientists interested in making sense of schizophrenia’s conundrums.
I love her. I like to go outside and rollerblade with her. I love when she comes over to see me. I also go bowling with her. I like when she makes me a name tag, like Dr. Greene’s on ER. I like to watch doctors on TV and talk about them with Lauren. I miss her and can’t wait for her to come home from Malawi.

Twelve-year-old Sam Ford's response when asked what he thought of Pitt med student Lauren Weintraub, MD '01
After a medical emergency, 10-year-old Sam Ford was put on a new medication. Almost immediately, his mother, Debbie Ford, started noticing changes in her son, who has a genetic syndrome that causes developmental disabilities and other problems.

The boy started eating more and gaining weight, putting on a pound a week. He was no longer interested in running on the home treadmill, which he used to love. He began crying over little things that had never before bothered him. For the first time in his life, he got into fights on the school bus and was in danger of being kicked off. [Family members’ names have been changed in this story.]

The changes were so disturbing that Debbie Ford expressed her concerns at her son’s next doctor’s appointment. The physician spoke to her only, while the boy, full of energy, ran around the room.

Photography | Julia Marous Straut
Are you not aware that your son is disabled? the physician asked. You’re not being realistic. Your son is very handicapped.

On the drive home, Debbie Ford began to wonder if the doctor was right. Maybe she was unrealistic about her son’s capabilities. Maybe the changes in his behavior were unusual. Then she asked about the doctor’s comments: Why did he say those mean things about me?

Lauren Weintraub, who graduates from the University of Pittsburgh School of Medicine this spring, was not in the doctor’s office that day. She soon, however, heard the story from Debbie Ford. She had been visiting the young Ford, who is now 12, and his family since she started medical school. She got to know him through Pitt’s Area of Concentration (AOC) in disabilities medicine. The boy is her “community mentor.”

Weintraub will tell you, she’ll be a better doctor for knowing him.

In the AOC program, students choose to go above and beyond the regular medical school curriculum. They gain in-depth exposure to one of six fields. Weintraub chose the disabilities medicine component; she might have instead selected women’s health, geriatric medicine, underserved populations, medical humanities, or bioinformatics.

“The idea is for the AOCs to cover specific topics in greater depth than they are covered in the curriculum,” says John Mahoney, director of the Office of Medical Education. Students take on a research project, one or more rotations focusing on the special interest, and other activities, which vary depending on the AOC. Most of the AOCs, for example, incorporate some type of community involvement, like the community mentorship, which is part of the disabilities medicine program. Students in the medical humanities AOC take two graduate-level Arts and Sciences courses and attend a national bioethics and humanities conference.

Besides Sam Ford—who calls Weintraub his best friend and has asked her to marry him—Weintraub’s favorite part of the program may be the journal article reviews, which are part of most AOCs. During these sessions, students critically discuss articles from the medical literature with faculty members.

“Our journal club is something that I really love,” Weintraub says. “It’s a time when all of us who have this interest get together and talk about what we feel should be done.”

Many of the AOCs also ask students to keep their own journals as a way of reflecting on their clinical experiences.

One might wonder why a med student would take on any of this—adding an AOC to an infamously demanding school load. According to Weintraub, it has not been a burden. In fact, she never questioned whether she would pursue the AOC.

“I was just so excited that there were other people who had this similar interest,” she says. During her first two years of science course work, the AOC helped Weintraub, who enjoys interacting with patients, focus on why she came to Pitt:

“It made all four years of my medical school a wonderful experience, because I was always able to keep myself motivated towards that time when I would have patient care responsibilities.”

Weintraub also appreciated the chance to differentiate herself—all medical students at Pitt take the same classes for the first three years, choosing electives only in the fourth year.

“The AOC is a way to show a side of yourself very early on,” she says.

Such is the spirit of the program. Each AOC was created in response to student or faculty interest. School administrators want to build AOC programs that center on a theme yet cut across disciplines.

Last fall, Mahoney, working with Joan Harvey and Steven Kanter of the dean’s office, helped design an exhibit about AOCs for the annual Association of American Medical Colleges conference. The program was received as novel—and with an enthusiasm that leads him to believe it will soon be imitated elsewhere.

When he was 16, Brad Dicianno, MD ’01, started working at a summer camp for children with muscular dystrophy. He went back every summer until he started medical school four years ago, at the age of 22.

“We got kids who were in wheelchairs to ride horses, to go canoeing, to go fishing,” he says. “It was such a magical experience for me. It was just a little world in and of itself. Our motto was, ‘Anything is possible.’ And anything the kids wanted to do, we would try our best to find a way to do it. To me, it just seemed like the real world should be like that.

“Life for people with disabilities isn’t really like that, and I want it to be.”

Now Dicianno spends a lot of time with Pitt physicians who are working, in their own ways, to make the world the kind of place he envisions.
Like Weintraub, Dicianno is completing the disabilities medicine AOC. And like all AOC students, he has paired with a professor who works in his area of interest. In the regular curriculum, medical students spend a month learning from a particular faculty member before moving on to new courses, new rotations—new professors. Dicianno has met regularly throughout medical school with Michael Boninger, an associate professor of physical medicine and rehabilitation, and has had contact with other professors who share his interest in disabilities medicine.

“Being involved in this AOC gives you a whole set of people who can give you insight into what their jobs are like and give you guidance,” Dicianno says. Boninger, as his primary faculty mentor, gave Dicianno advice about electives and residency programs and helped him set up a week-long shadowing experience. Boninger also encouraged him to participate in a national student research competition. Dicianno won first place—twice. “When I decided that I wanted to go into physical medicine, knowing Dr. Boninger so well made things a million times easier for me,” he says.

Dicianno now plans to be a clinician, researcher—and teacher. “Academics are a good way to change the world,” he says. “So many physicians are lacking in their knowledge in this area [disabilities]. I’d like to be involved in changing that.

“The AOC helps you find out who you are and what you want to do with your life.”

Much to his mother’s relief, Sam Ford lost weight and his usual personality returned after a new physician prescribed a different medication. Later, when Lauren Weintraub asked him what he thought about the other medication he had taken, he recognized the pharmaceutical name immediately, and said, “Oh, I don’t like that stuff.”

“He was aware of what was going on,” Weintraub says. “He is very sensitive to the way that he is treated by physicians.”

Physicians, Weintraub points out, don’t go home with patients after they leave the hospital or clinic. They never know what the patients think or say as they are driving home after a visit to the doctor. They don’t observe—day to day—the impact of an illness.

Yet that information is revealing, says Heidi Feldman, who directs the disabilities medicine AOC. “One of my philosophies is to try to get medical folks collaborating with human beings who have the condition,” says Feldman. “By dint of being a person with a disability or a family member, you are a teacher, because you can teach about your story.”

Hence Weintraub entered into a relationship she’ll never forget—though she has not yet accepted the boy’s marriage proposal. “I’ve been to religious services with his family a couple of times,” she says. “I’ve been to the doctor’s office with him. I’ve gone with him to his softball league for kids with developmental disabilities.” Even Weintraub’s parents...
have met Ford. She’s gotten together with the boy, on average, once a month during her four years in school. That average includes a semester during which she spent several weeks completing a clerkship in Malawi.

Learning about the boy’s experiences led Weintraub to reflect on how she wants to practice medicine. “It requires some extra effort on the part of the physician to give people with disabilities the care they deserve. I’ve seen that firsthand. And that extra bit of effort makes so much difference,” she says. That extra effort may mean, as it did in Sam Ford’s case, altering a standard course of treatment. The reactions he had to the medication are not known side effects of the drug. But children with disabilities that affect brain development often have unusual reactions to medications.

“The AOC has really taught me a lot about how to approach every patient as an individual, whether one has a disability or not. Every person has individual needs,” says Weintraub.

“Spending time with [Sam Ford] in his home and in the community, I’ve learned a lot about him that I realize I never could have learned in a doctor’s office,” says Weintraub, who will begin a pediatric residency in July. “This is probably the only opportunity I’ll have to really learn about a child like that.”

She has learned, for example, how people often underestimate Ford’s abilities. If someone asks him what he saw after he returns from a trip to the mall, he gets flustered and can’t answer. But weeks later, he may start talking about the mall. His mother says that Ford has to come up with the memories on his own; he might not be able to articulate an answer on the spot. Yet, on a given day, he might start describing events that happened years earlier, like a family trip to Disney World, in minute detail. The uninitiated assume that when Ford doesn’t answer a question, it’s because he doesn’t know or can’t remember the answer. “The truth is, he remembers better than any of us ever will,” Weintraub says. “I’ve been amazed by his memory. He’s such a fascinating person.

“He has really taught me a lot about how there’s more than just our traditional way of learning and how we really pigeonhole people’s intelligence.”

Released from the hospital with nowhere to live: This was a problem shared by many of those who found themselves staying at the Orr Compassionate Care Center in the East Liberty section of Pittsburgh. Every week, a half-dozen or so residents of the center would gather for a self-help group. The two- or three-hour meetings were planned and led by Elizabeth Cuevas (MD ’01), in conjunction with Sister Pat Mahoney of the center. “The residents would start discussing how they were abused as children, how their drug and alcohol problems affected their lives,” says Cuevas. “They would talk about their incarcerations, their stays in mental facilities, the times they were sleeping on the streets.” Hearing their stories was a privilege, says Cuevas. “It opened my eyes that there’s so much more going on in a person other than a medical problem,” she says. Cuevas led the groups as part of the medical school’s Area of Concentration in underserved populations. —DH
In the University of Pittsburgh Department of Surgery, they are tracking a phantom suspect. This ghost has given former presidential candidate Bob Dole a new career in TV commercials. (It is the basis for Viagra, the much-hyped magic potion for erectile dysfunction.) It also appears to play a key role in virtually every aspect of everyday physiology, from control of
blood pressure to wound healing to microbial infection, even to childbirth.

Therapeutic applications have saved lives in the operating room and given support to those with breathing problems. It also may help dialysis and coronary-bypass patients.

Yet this phantom comes and goes before it can readily be detected.

As molecules go, nitric oxide, or NO, is both elusive and unique, which helped it remain terra incognita until recently. Most substances enter cells via specific receptors on the cell’s surface, as a key fits into a keyhole; nitric oxide needs no receptors. It does its work as a gas, readily passing through the permeable cell barriers. NO also has an extremely brief half-life, a mere six seconds. It materializes in quick puffs and is gone soon after.

The molecule has captured the imagination of thousands of researchers. A torrent of 30,000 (and counting) NO papers has poured out of laboratories, mostly in the last five years; Science magazine crowned it “Molecule of the Year” in 1992 and an Indian journal upped that to “Molecule of the Millennium.”

Much of the basic biology of this ghost substance has been unveiled, surprisingly, at the laboratory benches housed in a surgical department—Pitt’s, to be exact. Former department chair Richard L. Simmons points out that surgeons’ research interests are normally pegged as short-lived. In a marked departure from that stereotype, the Pitt team has zeroed in on pure science as the best route to identifying NO’s benefits to patients.

“It is unusual,” says Simmons, who gave up the department chair in 1998 after 11 years, “for a surgery department to maintain such a devoted and unremitting focus on any problem in basic science.”

That dedication by a small group of surgeons has produced a series of research firsts. To name only a few of the most important, Pitt surgeons were first to show that NO could be made in human liver cells (previously it had been identified only in mouse immune-system cells); first to show that it was made also by the heart; first to describe its role in facilitating organ transplant rejection; first to show that it could be used for therapy in blood-vessel disorders. “And lots more,” Simmons says. Perhaps the two most attention-getting discoveries came in the early ’90s from Timothy Billiar, the tall, reserved Nebraskan who led the research effort at Pitt and last fall succeeded Simmons as department chair, and David Geller, now the Samuel P. Harbison Assistant Professor of Surgery and a faculty member at the Thomas E. Starzl Transplantation Institute. Billiar et al. identified the human gene that turns on inducible nitric oxide synthase (iNOS), which is a key enzyme for triggering production of NO throughout the body. Geller cloned the gene. That success opened the way for expression of a recombinant human iNOS. (Recombinant, meaning Geller applied the same gene-splicing technology—invented, in part, by Pitt grad Herb Boyer—that made possible treatments such as the now widely used form of insulin that has replaced animal-derived insulin. The other often caused allergic reactions in diabetics.) Pitt now holds four patents based on the cloned gene, and pharmaceutical companies worldwide are assiduously using them to pursue a wide range of therapeutic applications.

Oddly, although it combines the two most common elements in the earth’s atmosphere—nitrogen and oxygen—little was understood about nitric oxide as recently as 15 years ago. What was known cast NO as an environmental villain, a particularly noxious product of auto exhaust. In the days before catalytic converters were mandatory, for example, German foresters and Greens vociferously blamed auto-generated NO for killing the spruces and firs of the beloved Black Forest.

And yet physicians had been using nitric oxide therapeutically for a century without completely understanding why. That was in the form of nitroglycerin, a vasodilator often prescribed for angina pectoris (the acute chest pain that comes from heart muscles not receiving enough blood) and other cardiac conditions. Nitroglycerin expands the diameter of blood vessels and increases blood flow to the heart.

In 1977 Ferid Murad, a pharmacologist/physiologist at the University of Texas–Houston, discovered that nitroglycerin opened coronary arteries by releasing NO. He theorized that the body itself could stimulate the release of NO to regulate blood vessels. But he had no experimental evidence to back up his theory. Then in 1980 Robert F. Furchgott of the State University of New York Health Science Center at Brooklyn found that the endothelium, the inner lining of the blood vessels, released a substance that relaxed the vascular muscles and increased blood flow. He called the substance endothelium-derived relaxing factor, or EDHF.

It took six years more for Louis J. Ignarro of the University of California, Los Angeles, another pharmacologist, to capture the ghost. Ignarro, using spectroscopy, identified the relaxing factor as nitric oxide. Furchgott, Murad, and Ignarro received the 1998 Nobel Prize in Physiology or Medicine for discovering “an entirely new principle for signaling in the human body.”

In 1987, as Furchgott and Ignarro caught the attention of the scientific world, Richard Simmons came to Pitt from the University of...
Minnesota. Billiar, four years out of medical school, came with him as a research fellow. Simmons, “a transplanter by trade,” quickly saw that nitric oxide, with its ability to dilate blood vessels, might offer clues to one of the most dismaying and unfortunately all too familiar problems of the operating room—the postsurgical shock and loss of blood pressure that can lead to massive organ failure and death. Geller, who joined the effort a few years later, had more than once seen these devastating effects: “Patients get sick and then very sick and end up in surgical IC units; they develop sepsis or disseminated infection throughout the entire body, and go into multisystem organ failure, which eventually does them in; they succumb and die.”

Simmons explains how the research offensive came about. “I am a catalyst by nature—and curious.” He began to recruit a team to carry out the work.

“The power structure in the field of surgery is such that a chairman has tremendous power,” he says. “Therefore, people in the field with ambition tend to be drawn to the chair’s interests. A smart chair takes advantage of that opportunity. You get to choose the smart ones. You support the careers of the smartest and most productive and are rewarded for that in turn.”

By 1988, Simmons was starting to see the returns on his recruiting efforts in the form of research results; by 1993 he was flooded with NO breakthroughs. “We didn’t at first focus on NO,” Simmons says. “It just happened to be the answer to questions we were asking about organ failure in sepsis. That caused us to ask more questions. If you keep asking why, you sometimes are lucky.”

Nitric oxide actually plays a couple of basic roles in human biology, each of which is controlled by the expression of different genes. When it’s released by an enzyme known as constitutive nitric oxide synthase (cNOS), it often becomes a neurotransmitter, one of the chemical messengers that carries impulses from nerve cell to nerve cell. That enzyme is present in minute quantities in the body at all times to carry out this role. Other times, it’s turned on by inducible nitric oxide synthase (iNOS)—the enzyme Billiar and Geller have come to know about as well as anyone—and it is produced when the body is stressed by inflammation, say, or widespread infection. Then it is turned out in great quantity—up to 1,000 times more than when it’s produced by cNOS. This latter, often crisis, mode of nitric oxide is what has captivated Billiar and Geller.

Billiar led the way in unraveling the complexities of the molecule. As early as 1989, he was explaining that NO was derived from L-arginine, one of the amino acids that are the building blocks of life. He also identified the role of growth-regulating cytokines in the generation of NO. His curriculum vitae lists 24 pages of publications, almost all on NO, and nine pages of invited lectures.
After Timothy Billiar found the gene, David Geller (above) cloned it.

around the world. Within seven years he rose from assistant professor of surgery to associate professor to Watson Professor of Surgery to George Vance Foster Professor and chair of the department.

“Tim is recognized as one of the world’s leaders in this area,” Simmons says, praising his protégé. “He is always invited to meetings, national and international, on anything to do with NO—a testimony to the importance of his work.”

In contrast to Billiar, who is often so soft-spoken that you must lean forward to catch what he is saying, the ebullient Geller comes bounding from his office, hand outstretched. “I’m Dave Geller!” he says, without waiting for you to be ushered in by an assistant. He sits at a cluttered desk and scoops up a pencil-sized apparatus, clicks it, and hands it to his visitor. Tiny wire hooks pop out at the base.

“For radiofrequency ablation of liver tumors,” he explains, inviting the visitor to click it again and then pointing to the slender wires. “I’m a liver surgeon. I spend half my time doing liver transplants, half removing liver cancers. With this, we click it into a liver cancer and these 10 little tines, or hooks, come out and burn out the cancer. If we can’t cut ‘em out, we burn ‘em out.”

Geller is certainly a preeminent researcher as well as surgeon. He has 60 NO publications on his own CV, holds a career development award from the American College of Surgeons and a five-year $500,000 research grant from the National Institutes of Health (NIH). After conducting liver research at NIH, he came to Pitt as a 25-year-old intern, quickly immersing himself in the nitric oxide work. His iNOS cloning triumph came before he was 30. Billiar calls him “the world’s leading authority on the iNOS gene.”

Geller continually emphasizes the department’s view that, despite its commitment to basic science, Pitt surgeons remain surgeons first and foremost.

“My research interests stem from what I do clinically as a surgeon,” he says.

“Many problems we see in the operating room, if we could understand the pathophysiology or molecular biology and the basic mechanisms responsible, maybe ultimately we could find a way to prevent or find novel strategies to treat patients.”

Thus, the vexing problem of postsurgical shock remains at the top of the agenda for the dozen or so department “worker bees,” as Simmons calls the NO researchers. Billiar is the primary investigator (working with Bruce Pitt of environmental and occupational health, Tony Bauer of medicine, Brian Harbecht of surgery, Mitch Fink of critical care medicine, and others) on a major, nationally funded effort that’s looking into this complex problem. Department researchers are also investigating NO’s apparent role in apoptosis, or programmed cell death. “We are one of many labs all over the world looking into this question,” Billiar says, noting that understanding NO’s link is hugely important. “It’s a big field of research,” he notes. For instance, researchers think that understanding NO’s role in cell-death programming might lead to new cancer
Nitric oxide has an extremely brief half-life, a mere six seconds. It materializes in quick puffs and is gone soon after.

therapies down the road—however, no one knows how NO might halt cancer growth, it may actually stimulate it.

NO zaps infections as well; elsewhere at Pitt, researchers are studying how the immune system employs it in diseases such as tuberculosis (no one understands exactly how the TB process works). Also under investigation is NO’s possible role in neurodegenerative diseases such as Parkinson’s and Alzheimer’s as well as rheumatoid arthritis and osteoarthritis. Too much NO production triggered by inflammation may have a role in tissue destruction in arthritic joints.

On a more basic level, Geller is investigating, through an NIH grant, the on/off signals of the iNOS gene. “We have a fairly good idea of what turns on the gene. Almost nothing is known about the molecular mechanisms that turn off the gene. In certain settings you want to overexpress the gene because it would be beneficial; in other settings it would be clearly harmful, and you want to turn it off or prevent its being activated.” To give an example of an NO too-much/too-little tightrope walk that occurs naturally in our bodies: The cardiovascular system relies on a little NO to keep blood pressure in check, yet an excess can bring about catastrophic collapse.

A clinical trial of NO in kidney dialysis patients is in the startup mode, directed by vascular surgeon Edith Tzeng, assistant professor of surgery (who, Billiar says, in his low-key way, “happens to be my wife”). In dialysis, a U-shaped arteriovenous shunt linking arteries and veins is permanently implanted, usually in the arm, and blood is withdrawn via the vein, cleansed of water and impurities and then returned via the artery. The shunts often narrow and allow clots to develop, or they close up altogether and collapse within a year or so after implantation. In earlier research, Tzeng, with Pitt’s Larry Shears, had shown that NO inhibited the growth of smooth muscle in the vascular walls; it is this growth that reduces the diameter of the blood vessel and hampers blood exchange. In the trials, supported as part of a $14 million cardiac gene therapy grant, she will infuse the cloned iNOS gene when the shunt is implanted to determine if the vessels will remain open. Later, the investigation may be extended to coronary-bypass and angioplasty patients, whose vessels also may close some years after the procedure.

Reflecting on the NO furor of the past decade, Simmons notes that worldwide research interest in the subject has started to plateau. There is no sign of a slowdown at Pitt, however, where surgeons continue to chase the shadow.

William Kiester contributed to this article.
A

other lab meeting. Another standing-room-only crowd. They eagerly await the main attraction. He arrives, looking not quite the star. He wears no tie. Not even a collared shirt. In fact, his jersey still has hints of perspiration from his bike ride to work. As for his corduroys, there are a few strategically worn holes in the backside. The others, crammed into the room, are dressed more like doctors. For good reason. They are doctors.

But so is the man of the hour. He is Richard L. Simmons, and though his colleagues at the University of Minnesota might question his attire, they don’t question his intellect.

“He has a unique ability to connect ideas—to emphasize what is important and what isn’t important—and to synthesize a new concept out of those ideas,” says Timothy Billiar.

He should know. Billiar, Simmons’s successor as the University of Pittsburgh’s chair of surgery, was a research fellow in his lab in Minnesota. “People would flock to Dr. Simmons’s lab meetings,” he recalls, “to present in front of him or hear what was being presented, because they would get ideas.”

Simmons’s CV lists 16 books and more than 1,200 articles on topics such as transplantation, immunology, and surgical infections. His widely referenced *Surgical Infectious Diseases* (his coauthor is Richard J. Howard) was the first of its kind when it was published in 1982 and is now in its third edition. Meanwhile, during his 19 years at the University of Minnesota, Simmons helped direct its world-renowned kidney transplant program. He also led the US Army Surgical Research Team in Vietnam.

Since his recruitment here in 1988 by Thomas Detre, then the senior vice chancellor for health sciences, to lead the Department of Surgery, his faculty's research on nitric oxide (NO) set the stage for understanding the mysteries of this molecule. A host of new treatments have sprung from that understanding (including Pfizer's development of Viagra).

**“The history of surgery is the history of doing the wrong operation.”**

Perhaps most noteworthy—thanks to harnessing NO's ability to impede the narrowing of blood vessels—is applying NO to keep cardiac patients' blood vessels open after they've been dilated during surgery. Yet, rather than giving a standard press-release response concerning all those accomplishments, Simmons prefers to quote *Saturday Night Live* character Chico Escuela: “Besball bin berry, berry good to me.”

In 1998, at the age of 65, he stepped down as chair of surgery, but his workweeks have not lessened. Simmons is the University’s vice chair for surgical research and also medical director of UPMC (where he is in charge of patient safety, and where he has been converted to wearing a shirt and tie). When he bumps into one of his protégés these days, he’s still likely to ask, “What have you done today that will make me famous?”

He has been known to rub people the wrong way, however. Billiar remembers Simmons asking interns in Minnesota, “Why are you killing my patient?”

Though Billiar admits the half-comical, half-serious question offended some, he appreciated his boss’s point: “It was a way of making the doctors think very hard about what they had just ordered or done to that patient.”

It’s clear Simmons’s nontraditional thinking and actions—seasoned with a healthy dose of wit—are his trademarks. His style appealed to Detre during his search for a chair of surgery in the late 1980s. “Dick has a most engaging smile. He is self-deprecating; you would have the feeling he doesn't take anything seriously, most of all not himself. Now, for one of the most prominent academic surgeons in this country, this is unusual behavior,” says Detre.

He’s been counted among the “Best of the Best” by the *Archives of Surgery*; is a past president of the Society of University Surgeons, American Society of Transplant Surgeons, and Surgical Infection Society, among other elite organizations; yet there are no signs of ostentation on Simmons’s office walls. No awards or diplomas, even though Billiar reveals he must have crates full somewhere. “They’re in cardboard boxes in the basement,” admits Simmons. He would rather talk, however, about what he has instead chosen to hang on his walls: a collection of rare textiles. Most prominent is a century-old Ecuadorian poncho.
“I think it's beautiful,” says Simmons. He expatiates on its creation—harvesting the cotton, spinning the yarn, the tie-dye techniques used, the weavers, the embroiderers. . . . He knows so much about this piece; yet it's just one of hundreds in his collection. And that isn't counting the 1,000 or so textiles he has donated to the Minneapolis Institute of Arts.

Simmons is just as willing to chat about another unusual collection in his office—four bright orange aluminum chairs. As university office décor goes, they stand out like Nittany Lions in a room full of Panthers. They were recently featured in an aluminum exhibit at the Carnegie Museum of Art.

“I've always liked chairs,” he says, shrugging. “Chairs are like people, except they don't talk a lot. They have a front and a back, a history. These aluminum chairs, they are technically remarkable because the aluminum and the plastic are extruded together so there is no glue, no bolts, no joints, no dowels. It comes out as one piece. Terrific!”

His deep curiosity regarding a given artifact's design and history is a tip-off to what makes him such a significant scientist.

“Everything deserves investigation,” he points out. “The history of surgery is the history of doing the wrong operation. It has taken all kinds of investigations in order to discard these operations. And the history of medicine, in many respects, is the history of discarded therapies.”

“Dick thinks like an internist,” says Detre. “He somehow thinks that surgery has a momentary advantage in clinical medicine and our best hope is that we will acquire the necessary knowledge so we won't ever have to use the knife.” That philosophy isn't totally unprecedented for a surgeon. “I'm sure,” Detre says with a smile, “you would find two or three more like him out of the many thousands.”
no squadron of jet bombers can be seen swooshing below the ceilings of maternity wards. There are no echoes of antiaircraft fire reverberating off baby cribs, either. But the appearance of tranquillity is deceiving. There is an air battle of epic proportions taking place.

The enemy, in the form of flying bacteria, is everywhere, though invisible. Ground zero is the lining of the lungs, where the defense is situated.

Starting with every baby’s first breath, the combat begins. Inhaled bacteria seek to colonize the lungs by invading...
patients may dramatically improve because of Robert J. Bridges, professor and vice chair of the University of Pittsburgh School of Medicine's Department of Cell Biology and Physiology. Bridges, whose PhD is in physiology, and his collaborators have discovered a pharmacologic treatment designed to allow CF patients to mount a defense against bacteria and viruses inhaled as they take routine breaths.

This dramatic encounter occurs practically every time people swallow or clear their throats, except for the 30,000 children and young adults in the United States who have cystic fibrosis (CF). The bacteria eventually win the battle in their bodies. They die young—90 percent directly from pulmonary problems. Thirty-one is the median age of survival for people with this genetic disorder.

The life span and quality of life for CF patients may dramatically improve because of Robert J. Bridges, professor and vice chair of the University of Pittsburgh School of Medicine's Department of Cell Biology and Physiology. Bridges, whose PhD is in physiology, and his collaborators have discovered a pharmacologic treatment designed to allow CF patients to mount a defense against bacteria and viruses inhaled as they take routine breaths.
Ride secretion and its implications concerning life-threatening diarrhea.

In 1983, CF was characterized as a chloride transport disorder. Raymond A. Frizzell—who was the director of the CF center at the University of Alabama at Birmingham (UAB)—took notice. He sought out additional chloride transport experts to join his team. (Years earlier, as a postdoctoral fellow with Pitt’s physiology department, Frizzell had published his own breakthrough papers on chloride transport.) Bridges came on board to continue his own chloride channel research. In July of 1989, his research changed, thanks to the discovery of the CF gene (CFTR), by Lap-Chee Tsui, at the Hospital for Sick Children in Toronto, who worked with Francis Collins, of the Human Genome Project, and John Riordan. (Tsui happened to earn his PhD in biological sciences from Pitt in 1979.)

“Before the gene had been discovered,” Bridges recalls, “the chloride channel that I was working on in Germany was thought to be the most important chloride channel in CF. But as it turned out, when the CF gene was discovered in ’89, it wasn’t the right channel.” Naturally, he switched channels. Not everyone in the CF community followed suit, however. Now there were two ways to deal with CF: Try to devise a treatment to minimize its effects, as Bridges was. Or, try to fix the gene. Most researchers opted for the gene therapy approach—by a landslide.

“When the gene was discovered,” says Bridges, “with the publicity around it, some parents took their children off the lung transplant program, the waiting list, in anticipation that gene therapy was around the corner.”

Orenstein remembers the jubilation: “When the gene for CF was discovered in 1989, a lot of people said, ‘Well, we’re going to have a cure right away. We’re going to have gene therapy, and CF is going to be a thing of the past.’ But in CF animal models and in some patients, it looks like the efficiency of gene transfer has been lower than you would like, and the inflammatory response has been higher than you would like.”
Penland notes that the tricky part of gene therapy is, as he puts it, “getting the gene of interest into the cells of interest, and keeping it there.” He thinks overcoming these hurdles will take “quite a few more years.”

Bridges didn’t pursue the gene therapy approach, but he did consider the implications of the malfunctioning or missing protein.

To use a nonmilitary analogy, the role the CFTR protein plays can be compared to the job of a guy who takes care of a pool. If the pool man is dependable, he’ll do such a good job regulating the chemistry, the owners will notice nothing but cool lapping water. Likewise, a dependable CFTR protein controls the sodium-chloride fluid (pool) that coats our lungs, keeping them nicely hydrated. To push the analogy further, if the CFTR pool man is doing his job, that means a big one-way water volleyball game is on—the cilia being the teams that flick away the bacteria- and virus-laden mucus.

If the pool guy is sloppy or doesn’t show up, the pool chemistry gets strange. In the case of CF, what actually happens is this: The chloride is not secreted properly through its channels within the epithelium, so it isn’t able to use its chemical properties to pull sodium and water along to the lining of the lungs. That means the pool can’t fill up properly in the first place. To make matters worse, the cells’ sodium channels (imagine a bunch of drains in the pool) start working overtime, sucking the sodium back into the epithelium; the chloride and water follow. That empties the pool.

When the lungs are dehydrated, the cilia lose their ability to spike the mucus. Coughs, sneezes, and swallows are of little help; the cilia are doomed to be crushed by the weight of the goo. Eventually, bacteria colonize in the lungs, and lethal pulmonary conditions are likely to develop.

Researchers take lung cells from transplant patient tissue, grow them on filters, then place them in the above chamber to test the cells’ response to various compounds.

Bridges searched for a pharmacological answer to the dehydration problem. For years, he continued to focus on the chloride channel in hopes of developing a compound that would assist its secretion.

Then, in the early 1990s, a team of Swiss researchers pinpointed the type of channel, ENaC, responsible for sodium transport. That got Bridges to switch channels again. He shifted his focus, delving into the complexities of the sodium channel. (Remember the drains that work overtime?) Yet, as with any lung cell biology experiment, he and the other UAB investigators needed a rare commodity, lung tissue. The University of Pittsburgh performs on average 47 lung transplants annually, seven on CF patients. Largely on the basis of that kind of tissue availability, Frizzell, Bridges, and 15 others from the CF center at UAB relocated to Pitt’s Department of Cell Biology and Physiology in 1995. Within two years, the school had established its Cystic Fibrosis Research Center. Frizzell and Bridges serve as codirectors.

Since making the trek north, the researchers from the UAB group have remained close, meeting almost daily for lunch. They often treated themselves to outings at a student-friendly Tibetan restaurant along Forbes Avenue in the heart of Oakland (which has since closed). For this crowd, the backdrop of minced mutton, steamed buns, and sweet tea was preferable to any water cooler for swapping stories. The café also lent a relaxed air to musings on their research, what an outcome might mean, where to go next. . . . Frizzell says it must have been during one of those curry-inspired discussions that he mentioned to Bridges an interesting paper he’d just read. It had been published in Nature (10/9/97) by those same Swiss researchers who’d identified ENaC. In that paper, the Swiss described how they controlled sodium channels in renal epithelial cells with a compound made from cows, called Aprotinin. Aprotinin is a protease inhibitor, which means it can stop enzymes from splitting proteins (and in the case of CF, stop them from letting fluid pass through).

From that article, Bridges deduced it might be possible for such a compound to control the movement of sodium in the pulmonary epithelial cells and, importantly, the fluid that follows closely behind.
When Bridges began his Aprotinin experiment, it was clear that particular compound would never be a remedy for CF patients.

“Aprotinin is antigenic,” he explains, “so you can only use it once on a patient because the patient will develop antibodies to it.” If a patient is treated with it more than once, it’s likely to induce shock. And CF patients will need more than one dose, whatever the drug. Genetic disorders such as CF call for ongoing treatments, since the medical condition is embedded in the DNA.

Aprotinin couldn’t be the answer, but it could lead to an answer if Bridges’s experiment demonstrated that the protease inhibitor controlled the sodium channels in the epithelial cells lining the lungs.

It did. Bridges remembers that feeling of quiet euphoria in his lab as he monitored the results: “More than anything else, it confirmed that I was thinking properly.”

Next, he reasoned, he would have to find a protein similar to Aprotinin that wouldn’t elicit antibodies. He tried another protease inhibitor compound, but it didn’t control the sodium channels. He tried another. He tried quite a few. None worked.

“Finally,” he says, “I asked myself, ‘What makes Aprotinin so special?’”

He scoured the most esoteric of medical literature, hoping to discover the magic of Aprotinin. Three months later he found that magic in an amino acid sequence that distinguishes Aprotinin from the other protease inhibitors. The sequence is known as the Kunitz domain.

Bridges immediately did a PubMed search looking for a protease inhibitor that wasn’t antigenic, but contained the Kunitz domain. From that, he was able to identify an existing compound that looked like it fit the bill.

The compound is a human-recombinant protein equivalent to Aprotinin. Bridges garnered a sample; then conducted a test on transplant patient lung tissue. It worked. The compound inhibited the sodium channels, and fluid remained atop the lining of the lungs for several hours. (Other researchers had been working with another sodium inhibitor, the effects of which lasted just a few minutes.) Bridges had found a way to keep the pool filled and the volleyball game on.

This meant that perhaps one day, by periodically inhaling this compound—much as one might take asthma aerosol medication—CF patients would breathe more freely. The compound holds the most promise for CF patients who can begin the treatments early in their lives, or those with moderate pulmonary damage, since the approach still relies on the cilia to be strong enough to flick off the mucus.

Clinical studies will begin later this year. Orenstein—whose CF center at Children’s Hospital has about 400 patients—hopes Pittsburgh is chosen as a site for the trials.

“'The buzzword in medicine these days is bench-to-bedside. We have the perfect setup for doing that. Those guys [at Pitt’s CF Research Center] are great at the bench, and we have a lot of experience at the bedside.”

No matter where the trials are held, Penland will be watching enthusiastically from his CF Foundation office in Bethesda: “With the caveat that inhibiting sodium absorption is going to have a positive effect on the lung functioning of CF individuals, there is no question the compound has real potential.

“If the clinical studies go well, I don’t see why it can’t be a viable treatment option within seven to 10 years.”

PROTEIN POWER

If you don’t have cystic fibrosis, the more you learn about the disorder, the more you’ll be amazed by how deceptively simple it seems to be to keep your airways clear.

Neil Bradbury, assistant professor of cell biology and physiology, is one of several at Pitt delving into the intricacies of the disorder. He made a splash when he figured out the pathway by which the CF protein, called CFTR, is moved out of the plasma membrane of cells lining the lungs and the intestinal tract. He determined that the protein has sort of a zip code, defined by a sequence of amino acids that helps it be recognized and removed from the plasma membrane. (This is during the process that cells use to obtain and pass material through a cell, known as endocytosis.) This zip code, however, tells not only where the protein should go, but when it should. What does that matter? you ask. Well, how long CFTR decides to hang around the plasma membrane can make you feel a lot better or a lot worse. The protein is the means by which the membrane is hydrated; in the case of your lungs, it allows cilia to stay buoyant and flexible enough to repel mucus that would otherwise become fertile ground for bacterial growth.

And if you don’t have as many CFTR proteins in your plasma membrane as your body needs, that spells trouble. The protein creates a critical chloride channel that siphons the hydrating fluid from the cells onto the outer membrane. In some CF patients, these channels are prematurely removed from the plasma membrane. Bradbury thinks he knows why. He has discovered that sometimes the CF gene is mutated so that the body alters the rate at which the protein is removed. By understanding how cells recognize the zip code, he hopes to hide the code from the cell and keep CFTR in the plasma membrane, where it’s needed. —EL
The late Robert Egan, MD '50, considered one of the fathers of modern mammography, claimed America's peculiar attitudes toward breasts in the middle of the 20th century hampered advancements in cancer research, diagnosis, and care.
A woman with inoperable breast cancer stood before a group of medical students, residents, and professors, her breasts so large and dense that no current technique could tell them how big or deep her tumor really was. This was in the spring of 1956, at the University of Texas M. D. Anderson Cancer Center in Houston. As the woman stood there, Gilbert Fletcher, the head of radiation oncology, looked toward Robert Egan, a radiology resident who had received his MD from the University of Pittsburgh in 1950.

You're a diagnostic radiologist now, he told Egan. Why don't you figure out how to get X rays of breasts like these so we can know what we're dealing with?

Egan said nothing, but his curiosity was piqued, especially because a visiting fellow, Jean Pierre Batani, from Paris's Curie Foundation, was at the meeting with a breast X ray showing white flecks indicating cancer. Batani suggested that the technology might be helpful in cases such as the patient under discussion. However, as a radiation therapist, he had no knowledge of the technical factors employed. The technique, in the
few places it had been performed, was often far from polished. The images were likely to be fuzzy and grainy, and the balance of radiation level and voltage wasn’t right. When the X ray did produce something telling, as in the French example, no one was able to replicate it. Fletcher wanted Egan to find the right technique and make this tool a reality. Egan, who would become known as one of the fathers of modern mammography, obliged, setting off with no idea where to start.

Fletcher had picked a man with the temperament and persistence to rise to the challenge. As Egan reached school age in the 1920s, his mother shuttled him off to first grade in a one-room schoolhouse in their small Arkansas town. He came home a few hours later announcing that school was boring. The alphabet didn’t hold the interest of the young boy who’d already learned to read. So he stayed home through all of first grade, refusing to go until school had something to teach him. The first day of second grade, he gave it another shot, but it didn’t last: still too boring. It wasn’t until the third grade that Egan deemed school worthy, and once he arrived, his teacher bumped him to fifth grade. The impatient student finished college at 19, then became a metallurgical engineer and went to work in a Pittsburgh steel mill. Camped in front of a scalding laboratory furnace for 24 to 36 hours at a time, tinkering with temperatures to find the precise settings needed for specific batches of steel, Egan refined the art of trial and error. And after he walked away from his conversation in the hallway with Fletcher that big Texas spring day, he would rely on his well-honed art once again.

Though X rays were first used on breasts in 1913, mammography hadn’t grabbed the attention of the medical field because it was not yet a reliable tool. There were no precise images or techniques for technicians to replicate, and many thought it would never prove useful. Instead of pursuing radiology, others developed techniques like transillumination, which amounted to doctors pressing bright lights to their patients’ breasts as they stood in pitch black closets, hoping tumors would alter the beam of light as it passed through the tissue. But the technique was less than effective and risked charring skin—this was in a day that women already shied away from breast examinations.

Egan set out to develop a technology he knew nothing about, in an era when breasts were considered taboo. Americans’ attitudes toward the organs were steeped in paradox. Though movie fans were swarming to the cinema to see their favorite voluptuous Hollywood icons, and “sweater girls” were turning heads, many women blanched at the idea of doctors discussing or touching their breasts. Likewise husbands and fathers cringed at the thought of men examining the breasts of their wives and daughters.

“That was part of our culture back then,” says Gerald Dodd, emeritus professor and chair of radiology at the University of Texas M. D. Anderson Cancer Center. “You didn’t talk about breasts, and women weren’t comfortable bringing problems to their doctor’s attention because they were afraid it would lead to an examination, which most didn’t want.”

Egan was known to grumble about men making breasts taboo while glorifying their importance for sexuality and beauty. When he started out, few others were developing technologies for improving breast health. Jacob Gershon-Cohen of Albert Einstein Medical Center, in Philadelphia, Pennsylvania, was another path-setter in clinical mammography who’d run into his own roadblocks. And, of course, Pitt gave rise to at least one other breast cancer pioneer: As Egan set out on his quest for

better breast imaging techniques, Bernard Fisher, MD ’46, now a Distinguished Service Professor at Pitt, began his research here that led to the discovery that lumpectomies combined with radiation therapy were as effective as mastectomies for many patients.

Egan wasn’t deterred by the unpopularity of his endeavor, though he described himself as “hidden away” with his X-ray equipment, adjusting radiation levels, power, and film type. He developed methodical strategies for testing each possible variable as he x-rayed everything from paper clips to talcum powder, attempting to find the perfect settings and film.

After countless tries, Egan found the ultimate film—one he likely used in his steel mill days. It was an industrial product used for x-raying metal joints in pipelines. He also found the optimal X-ray settings. The voltage had to be high enough to penetrate a soft tissue like the breast, but much lower than that used to penetrate something as dense as bone. And the flow of electrons running through the machine had to be set high enough to get proper radiographic exposures.

Egan used inanimate objects as well as human subjects to find the perfect positioning of the breast by trying everything from compressing the breasts to “floating” them in liquid. Soon, his technique amazed colleagues by pinpointing cancers so undeveloped they were otherwise undetectable. But instead of being greeted with encouragement and acceptance, Egan met a wall of resistance from physicians and surgeons around the country who taunted him; some even called him the “titty man,” as one possible variable as he x-rayed everything from paper clips to talcum powder, attempting to find the perfect settings and film.

After countless tries, Egan found the ultimate film—one he likely used in his steel mill days. It was an industrial product used for x-raying metal joints in pipelines. He also found the optimal X-ray settings. The voltage had to be high enough to penetrate a soft tissue like the breast, but much lower than that used to penetrate something as dense as bone. And the flow of electrons running through the machine had to be set high enough to get proper radiographic exposures.

Egan used inanimate objects as well as human subjects to find the perfect positioning of the breast by trying everything from compressing the breasts to “floating” them in liquid. Soon, his technique amazed colleagues by pinpointing cancers so undeveloped they were otherwise undetectable. But instead of being greeted with encouragement and acceptance, Egan met a wall of resistance from physicians and surgeons around the country who taunted him; some even called him the “titty man,” as they snickered at his work.

He refused to give up. Egan packed his wife and daughters into his dark blue 1950s Ford sedan, filled the leg room in the back seat with clothes and food, and headed across Texas to teach other doctors what he knew about mammography. While their wives cooked and children played, Egan and the local doctors headed to clinics equipped with X-ray machines. He taught them to examine breasts properly and spent countless hours testing and critiquing doctors and technicians on all aspects of mammography: film technique, positioning, radiation dose, the works. Slowly, experience made them into believers. Physicians began requesting mammograms for their patients; and on three different occasions, shortly after doctors learned the “Egan technique,” they discovered breast cancer in their own wives.

Egan was not one to let escape any opportunity to sell his approach. Ed White, who was chief of surgery at M. D. Anderson, grew convinced after repeated impromptu conferences with the adamant radiologist. White would sit on a wooden bench in his surgical scrubs, smoking, with his head propped in his hands, as he and Egan discussed breast cancer and diagnosis. Later, in front of thou-

“... women weren’t comfortable bringing problems to their doctor’s attention because they were afraid it would lead to an examination, which most didn’t want.” — Bernard Fisher, MD

“Egan was the man who developed a smooth-riding automobile compared to a Model T,” Dodd says with a chuckle. “He put mammography on the map and made it an intelligible, reproducible study. In short, he was the father of modern mammography.”
98.6 DEGREES

People and programs that keep the school healthy and vibrant

GENEROUS ENTRÉE

MCMASTER SCHOLARSHIP
BY ELIZABETH A. MAY

On a rainy January night, Gilbert B. McMaster pulls up his white station wagon to the activity center entrance to let his wife out under the covered walkway. Once inside, Margaret McMaster doesn’t have to wait long before her escort of 54 years appears, a bit damp, but at ease in his tie and tweed sports coat.

They walk back to table 42 in the dining room. Some evenings, they eat alone; other nights, they’re joined by old friends or new acquaintances at Sherwood Oaks, a retirement community in Pittsburgh’s North Hills. On this night, over lamb chops and collard greens, the McMasters travel back to a time when Pittsburgh’s steel mills were gearing up for World War II, and Gilbert was embarking on his medical career.

In 1939, McMaster graduated from the University of Pittsburgh School of Medicine. Now 87, he still recalls the trek from his parents’ Mt. Lebanon home into Oakland for class. He would pack his mother’s car full of other Pitt and Carnegie Tech students, all happy for the ride.

McMaster didn’t really come to medicine; medicine came to him. Growing up in the home of a physician, he simply assumed he too would be a doctor. His father, Gilbert C. McMaster, earned an MD from Pitt in 1903. His diploma bore the stamp of John Brashear, acting chancellor of the Western University of Pennsylvania (as Pitt was then known). The elder McMaster practiced general medicine.

What started out for McMaster as a calm assumption turned into true professional zeal. Trained as an anesthesiologist, he approached wartime and peacetime assignments alike with the same quiet determination. McMaster served as a battalion surgeon during World War II in Hawaii, Okinawa, and the Philippines. During the Korean War, he was called to duty at a military hospital in Virginia to care for long-term casualties. In more peaceful times, he practiced throughout the Pittsburgh area.

He has a wish: that future MDs will always answer the phone as he did in the middle of the night, saying, “Yes, I’ll be there,” no matter where needed. To give a boost to Pitt students starting out their careers, the McMasters recently made a planned gift commitment to establish the Gilbert C. McMaster (1903) and Gilbert B. McMaster (1939) Scholarship Fund.

“We gave because we think Pitt is an important part of the community,” notes McMaster. “We felt a scholarship fund was most appropriate, considering the debts these students rack up.”

It’s time to bid good-night in the dining room, so McMaster fetches the station wagon, then guides it around the curves and dips leading back to their apartment. Sherwood Oaks lacks the intensity of the operating suites in which McMaster spent so much of his life. And the North Hills is far removed from Okinawa. It has been nearly 20 years since this doctor’s hands administered relief to a patient. On this dark and slippery night however, his touch at the wheel still is swift—and sure.

BORDER CROSSINGS

RESEARCH FRONTIERS
BY MARK JACOBS

Yet. The tour leader said “no,” then said it again. The border guards between Belarus and Russia were trying to extort a bribe, a little jackpot for themselves, before they would let the tour bus cross. In the meantime, the passengers could go nowhere, only wait. Hours later, the answer was still no, yet, until at last the guards gave up, and the bus moved on.

Jack Hoornstra, a passenger on that bus, has more pleasant memories from that trip. The Hermitage in St. Petersburg, for instance, was really something, he and his wife, Irma Hoornstra, agree. There have been so many wonderful trips together, through Great Britain, Holland, the Mediterranean. Better than memories, though, is the fact that they went at all. Hoornstra, 80, a former quality control engineer, has been through some rough crossings of his own.

“Do you have the rest of the afternoon? We can talk about Jack’s medical history,” says Irma Hoornstra, 79, a retired RN. She’s only half joking: “I have it written down in a book, and when we go to a new doctor, we hand him that.” An abstract of the procedures he has undergone over the years includes triple and quadruple bypass operations, a gastric resection—the list unfurls from there.

Good medicine—and often new medicine—has pulled Hoornstra through and allowed the couple to travel extensively and enjoy retirement years since moving from Erie, Pennsylvania, to Florida 20 years ago. To reward that good medicine, the Hoornstras recently gave the University of Pittsburgh School of Medicine $50,000, earmarked for research. Charity is not new for them. They have donated to Pitt’s School of Education (Hoornstra’s alma mater) and helped Habitat for Humanity build houses, among other volunteer efforts. Perhaps if those border guards had pleaded for a worthwhile cause, the Hoornstras would have convinced their tour leader to say instead, Da.
The teenagers, dressed in jeans and khakis, step toward the lighted viewer, looking at an X ray of a premature infant. Jon Watchko, professor of pediatrics, tries to dispel their hesitation. “You can come closer. I won’t bite you,” he says.

“They did an X ray like that on my sister when she was two weeks old,” says Ayonna Johnson, a confident 15-year-old whose hair is pulled into a ponytail.

“My guess is your sister was a little bigger than this,” says Watchko. “You can imagine what this baby is like.”

“That’s the actual size?” asks one girl.

The X ray shows the infant’s torso as no bigger than Watchko’s hand.

Johnson pays close attention. Her career goal is to work in a neonatal unit or as a child psychiatrist. The 10th-grader attends South Vo-Tech High School, where she takes courses in anatomy and physiology. She is certified to perform CPR, and she wants to learn even more. Two nights a week, she comes to the University of Pittsburgh School of Medicine. Wednesday nights she learns about pediatrics; Thursday nights, obstetrics and gynecology. She may come again next year to learn about other specialties. Tonight, at Magee-Womens Hospital, she’ll see a placenta and a premature infant weighing a little more than two pounds. She’ll learn about preeclampsia and fluid-filled cavities in the brain.

Watchko points out the baby’s lungs on the X ray. “Air on an X ray looks dark,” he explains. “Tissue is what causes this more light area. There’s a nice amount of air in the lungs here. I can tell that because it’s much darker.”

For “medical explorers” like Johnson, learning to interpret X rays is par for the course. The University of Pittsburgh School of Medicine’s Medical Explorers program, created in 1974, is affiliated with a national program established by the Boy Scouts. Pitt’s Explorers program seeks to increase the number of local disadvantaged and minority students—including African Americans like Johnson—who attend Pitt’s medical school. “If we can get the kids to say, ‘I can do it. It’s not beyond me,’ then we’ve got a chance,” says Robert Connamacher, director of the free program.

Six former explorers became medical students at Pitt. “Two of them grew up in the projects,” says Connamacher. Many explorers attend medical school elsewhere.

The program seeks to show students what medicine is really like.

“We do not clean up the act,” says Connamacher. “A while back, an ophthalmologist came and talked about the eye. Everything was fine. Then he showed a slide of an eye with a nail in it. All the kids went Ewwwwww! He turned off the slide machine. He said, ‘You’re a doctor. A patient is coming in here. He’s in pain. He has had this accident. He doesn’t know if he’ll ever see again. He’s coming to you for help. Are you going to look at him and say, Ewwwwww?’ That’s why I say this program is unique. I mean these kids in the past actually were stitching up eyes [in vitro].”

Only occasionally does the program fail to deliver the realism for which Connamacher strives. “We very often don’t get the smells,” he says. “The students are not in a position to lance an anaerobic cyst, which is the worst smell in the world.”

The explorers do meet minority medical students at Pitt—who participate in many of the sessions. Once a year, the med students take the teenagers to the anatomy lab, where together they study dissected organs. The explorers also meet specialists like Watchko, who lecture, give tours, or provide shadowing experiences. “We use the resources of the medical school fully,” says Connamacher.

At the X-ray viewer, Watchko shows film of another premature infant. “How old is that baby?” Johnson asks. Tonight, she’ll ask many questions, but her favorite part of Medical Explorers so far was the anatomy lab.

“You get to deal with real organs instead of just looking in a book,” she says of the program. “That’s really cool.”
TRULY, SIGMUND . . .

Paul S. Caplan, MD ’36, leans across the desk in his Oakland office, an eyebrow raised. “If Freud were my patient,” he says, “I’d be overwhelmed, speechless.” His hands are clasped, cufflinks clink and shimmer. Files sit in neat boxes on the floor—work to do. His fedora and trench coat lie carefully placed on a chair. On the wall, afternoon sunlight floods a painting of Jerusalem. Then, with the ardor he has for medicine, for people and their truths, he leans in and asks a question, one he hopes will take him beyond the bellyache, or back pain, to a place a disease is sometimes born—the psyche. “Well, truly, Sigmund,” he would ask, “what can you tell me about your father?”

As a physician with the Pittsburgh Symphony Orchestra for nearly two decades, Caplan traveled the world. However, before he worked with the symphony, he went to China with a group of physicians, to rural areas perhaps never visited by Westerners. And it was not the wall nor the isolation of the place that interested him. Rather, it was meeting with country doctors. “Years ago,” he explains, “preachers traveled from city to city ministering to people. In China, there are doctors who do the same. I spoke with one. Learned about traditional medicine, how they treat patients, took a look at their pharmacies. Fascinating.”

He shakes his head, “Fascinating stuff.”

Caplan was born before the First World War and served in the Second, listened to Jelly Roll Morton give way to Charlie Parker, watched streetcars grow rickety, and saw rockets take men to the moon. And though interested in these worldly evolutions, and though he and his wife of 58 years, Gertrude Caplan, have supported heartfelt causes through the years (including a generous gift to Pitt’s Arthritis Institute), his attention has remained duly focused on his profession and the people he serves. All else, beyond his family, falls, in gentle folds, away. At 88, Caplan, a rheumatologist, is perhaps the oldest Pitt physician still practicing. He still works 12-hour days, still goes on Friday rounds—three. He still reads 15 journals a week, keeps his hand in research, and visits Harvard each year for their advanced rheumatology courses. And with integrity and grace, he still attends to those patients he has been seeing 20, 30, 40 years. And he still makes house calls.

“I don’t think of it as work,” he says, looking for a file. “Work is something you have to do. This,” he says, spreading his arms, “is my avocation.” He leafs through a file. “I love what I do. I get to spend time with people.” He writes down a number, then looks up. “This woman, my patient,” he taps the folder, “I’ve been seeing her for 30 years. She’s in an assisted living facility.” He looks out the window. “I think I’ll visit her.”

It’s the whole patient, not the symptoms, not even the disease, which interests Caplan. He concentrates on the person, whose fear or frustration can turn acid into ulcers, or anger into chronic pain. And it is this holistic approach Caplan tries to teach third- and fourth-year Pitt med students who visit his practice as part of the curriculum. “They are in the trenches the first years, busy diagnosing the cause, the disease. But what they don’t always see,” he says, “is that disease is attached to a person, a person who sometimes needs to be attended to as much as the disease itself.”

It is quiet. Night has inched its way across Jerusalem. The work is not finished—he will take notes, scanning current journals for patients who need answers. Then, he will go to the home filled with art he and Gertrude have spent a lifetime collecting. He will walk past the cabinets full of cars his grandchildren once played with and go to his bookshelves lined with Freud. He will see what his wife has planned—a play, dinner with friends. Perhaps they will plan their next trip, a jazz cruise in October, a grandson’s graduation in May. Perhaps he will get on the phone, see how Charlie is doing, how Meg made it through the day. Or maybe, he’ll prepare quietly for tomorrow, for its patients, its surprises, and the questions left unanswered today.
CLASS NOTES

’50s  THOMAS J. TREDICI, MD ’52, has received the Louis H. Bauer Founders Award for his outstanding contributions to aerospace medicine and the Aerospace Medical Association. Tredici—who has taught more than 10,000 flight surgeons at USAF School of Aerospace Medicine, Brooks Air Force Base, Texas—is the first ophthalmologist to be so honored.

ALVIN MARKOVITZ, MD ’58, had two honors bestowed on him in recent months. He won the Presidential Award for Outstanding Teaching and Service from the American Academy of Disability Evaluating Physicians. He also accepted the Jericho Award for community service at the Los Angeles area Venice Family Clinic, one of the largest free clinics in the world.

BASIL RUDUSKY, MD ’59, presented his research study “Clinical Logistics in Treadmill Exercise Stress Testing” at the 47th World Assembly of the American College of Angiology, held in Orlando, Florida. He also gave the second opening address and was selected vice-president of the scientific council of the college by its board of trustees.

’60s  GILBERT L. FULD, MD ’62, has been named New Hampshire Pediatrician of the Year by the New Hampshire Pediatric Society. Fuld is an adjunct assistant professor of pediatrics at Dartmouth Medical School. He specializes in treating children with learning, attention, and behavior problems.

JOHN R. KRAUSE, MD ’66, was appointed chair of pathology and laboratory medicine at Tulane University Medical Center. He had been serving as interim chair since July 1999. Before going to Tulane in 1992, Krause spent 20 years here as professor of pathology and vice-chair of graduate medical education in the pathology department.

’70s  A. JAMES GIANNINI, MD ’74, among other appointments, is president of the Ohio chapter of the American College of Clinical Pharmacology and director of the Alumni Schools Committee for Yale University. He also has written two books: Drug Abuse: A Family Guide to Detection, Treatment & Education (1999) and Drugs of Abuse (1997).

ALLEN J. PALMER, MD ’74, is the training and supervising psychoanalyst for the Boston Psychoanalytic Society and Institute.

MARY MANCINI, MD ’78, joined the staff of eMedicine, an online medical education network (www.emedicine.com). Mancini serves as editor-in-chief for JAMA, has been elected to the Institute of Medicine.

’80s  LEE A. SHRATTER, MD ’83, a radiologist with the Kaiser Permanente Medical Group in Richmond, California, writes and edits the newsletter Countdown to Safety. He is a member of the American Medical Writers Association.

’90s  SCOTT V. JOY, MD ’92, has been promoted to assistant clinical professor of medicine at Duke University Medical Center.

SUZAN OBAGI, MD ’96, is a clinical instructor and cosmetic surgery fellow in Pitt’s dermatology department. Before finishing her residency here, she completed her medical internship at the University of California Irvine Medical Center, where she was named Intern of the Year in 1997.

And the winner of the 2001 Hench Distinguished Alumnus Award is, drumroll please, Ernest E. Moore Jr., MD ’72, professor of surgery at the University of Colorado Health Sciences Center. He will speak at the May 18 senior class luncheon.

GARY M. WILLIAMS, MD ’67, a professor of pathology at New York Medical College in Valhalla, New York, is one of the first nine fellows named by the newly formed International Academy of Toxicologic Pathology.

CATHERINE D. DEANGELIS, MD ’69, editor-in-chief for JAMA, has been elected to the Institute of Medicine.
THE WAY WE ARE

The year is 1991. Panther gridiron fans are climbing Cardiac Hill to watch what they think will be the last home game against Penn State.

Ten years later, there is no stadium atop Cardiac Hill and no Pitt-Penn State football game to look forward to, either. That annual pigskin classic, which resumed in 1997, has gone on hiatus once again.

For the CLASS OF ’91—which will have its 10th reunion on campus during graduation weekend (May 18 and 19)—there have been changes as well. Medical careers are now anchored all the way from the rocky coast of Maine to sunny California.

Tucked away a few miles from the Atlantic is Michael Albaum, MD ’91. The internist is medical director of PrimeCare, a 39-physician multispecialty group in Biddeford, Maine. Within that group is an obstetrician/gynecologist who was one of Albaum’s classmates. Tammi Bittler, MD ’91, and Albaum have something else in common. They’re married.

“I met her the first day of orientation. We have a family now, have careers; it was a very productive few years in Pittsburgh,” understates Albaum. Bittler is due to give birth to the couple’s second child on May 21, which understandably puts a crimp in their attending the class’s May shindig.

Lori Halaszynski, MD ’91, will be there, however. She won’t have far to go. The internist’s office is a 15-minute drive from the Oakland campus. In addition to her clinical practice and work with residents, she teaches medical students about physical diagnosis. “From a career standpoint, I’m pretty happy with my current situation. It’s a good mix of seeing patients and teaching. But I’m not married yet,” she says with a laugh. “That I thought would be different.”

Pittsburgh native Richard Juien-Dah Pan, MD ’91, has migrated to the West Coast. The ’91 class president is an assistant professor of pediatrics at the University of California, Davis. Based in Sacramento, he is involved in several health services research projects, including one that gauges the impact of consumer advertising for prescription medications.

“The issue,” he says, “is how does this increase health care costs for all of us by increasing demand for the latest and most expensive medications?”

Oh, and he won’t let 3,000 miles deter him from attending the upcoming reunion: “We had a great class.” —RM

IN MEMORIAM

’30S
WILLIAM J. HALL (MD ’35)
JANUARY 15, 2001

RAYMOND STEPT (MD ’35)
JANUARY 13, 2001

’40S
JOHN A. YOUNT (MD ’41)
OCTOBER 29, 2000

CARL J. PELOSSANO (MD ’43)
FEBRUARY 13, 2001

DAVID MENDELSON JR. (MD ’46)
JUNE 3, 2000

PAUL K. WELLMAN (MD ’47)
MAY 19, 2000

’50S
THOMAS E. COUCH (MD ’52)
MAY 7, 2000

FOSTER HAGES (MD ’52)
MAY 23, 2000

RAYMOND G. SCHMALE (MD ’52)
MAY 3, 2000

IRVIN M. GOLDING (MD ’54)
FEBRUARY 15, 2001

’70S
STEPHEN J. GABIN (MD ’73)
AUGUST 19, 2000

FACULTY
ALDO V. LONDINO JR.
DECEMBER 17, 2000

SAMUEL B. SALVIN
DECEMBER 8, 2000

ROMUALD J. CAROFF (MD ’55)
JANUARY 1, 2001

’70S
STEPHEN J. GABIN (MD ’73)
AUGUST 19, 2000

CALLING MD ARTISTS

Did you have a blue period? Or maybe a blue and gold period? We’re interested in exploring the links between medicine and art. If the muses have visited you, say in the form of pen and ink or oils, consider making a toll-free call to Jennifer Rellis. Among other titles she holds with the School of Medicine, Rellis may be the world’s first medical school art curator.

Call 1-877-MED-ALUM for details.
Iris South will not deliver her baby in a hospital delivery room even though there's one nearby. In labor, she rides past the hospital to the office of the family doctor who will deliver her second child, Jeannette. No other black woman can deliver in the local hospital, either. It doesn't accept blacks, any blacks, as patients. The nearest hospital that will, here in southern Alabama in the early 1950s, is 100 miles away, in Tuscaloosa. Fast forward to today, and Iris South's little girl is making her own mark on doctoring.

Jeannette South-Paul, MD '79, is circling back to a point halfway in her travels from Demopolis, Alabama. The graduate of the University of Pittsburgh School of Medicine is coming back to Pittsburgh as the new chair of the Department of Family Medicine. When she arrives in June, she will be the first woman to serve as permanent chair of a department here and one of a small number of African-American chairs in medical schools around the country.

Who she is and where she has come from will make themselves felt here: “Every time I walk into a room, the first thing I notice is who’s in the room. Not the number of people, but the makeup of the people. I will notice if there are no women in the room. I will notice if there are no minorities in the room. I will notice if those who are there appear to be treated differently. . . . On any project, I will ask, ‘Is there balance? Does everyone have a voice?’”

Her journey from the south had its beginnings in Jamaica, which her parents left to serve the Church of the Brethren as Bible class teachers and missionaries, first in Alabama, then New York, Iowa, Michigan, and finally Pennsylvania. In Philadelphia, the Souths, with six children, moved into the apartment above the interdenominational Helping Hand Mission they ran. The teenage South-Paul took charge of the thrift shop on Saturday mornings.

Her parents’ example evoked an interest in serving families, perhaps as a missionary for the Brethren or a social worker. Eventually, she decided to pursue medicine, so she received an undergrad degree in medical technology from the University of Pennsylvania. With an army scholarship, South-Paul went to med school here, where she was a leader in the group that established the Black Bag Award, which honors a faculty member each year for work with minority students. For the past several years she has served at the Uniformed Services University of the Health Sciences in Bethesda, Maryland, as a colonel, a professor and chair of family medicine, and the first vice-president for minority affairs. Among the broad range of research topics with which her name is associated: premenstrual syndrome, treatments for osteoporosis, infant nutrition, exercise during pregnancy, and sociocultural issues in health care.

“I want them to see Renaissance people.”

When South-Paul started going on rounds at the end of her second year at Pitt, she knew medicine had been the right choice. Seeing patients sealed her interest in family medicine even though she was encouraged by some to go into a higher-paying specialty—besides, family docs saw only colds and diabetes, they would say. But, to South-Paul, family doctors treated not a case of diabetes but Mrs. Jones who has diabetes—and maybe hypertension or coronary artery disease or cancer.

“You cannot divorce the science from people,” she says; and through the years, her choice has been confirmed by the “breadth and depth” she has seen in family physicians: “I want students at Pitt to know that family physicians can be researchers, they can be teachers, they can be clinicians, they can be citizens and administrators. . . . I want them to see Renaissance people.”

The first woman and the first black to serve as permanent chair of a Pitt med school department
We found these fellows in the 1955/56 Hippocratean (artist unknown). They have that look of being legends in their own time, and we're betting you know some of the lore. Send us your stories.
CALENDAR

APRIL 28
SECOND ANNUAL
PITMED GOLF OUTING
Meadowink Golf Club
Murrysville, Pennsylvania, 9 a.m.
For information
golfouting@pittmed.pitt.edu
www.pitt.edu/~asmt27

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

MAY 18
ANNUAL ALUMNI DINNER DANCE
Pittsburgh Athletic Association
Pittsburgh, Pennsylvania
For information
Ross H. Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

MAY 18
SENIOR CLASS LUNCHEON
Twentieth Century Club
Pittsburgh, Pennsylvania
For information
Ross H. Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

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

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

MAY 18 AND 19
CLASS OF '91 REUNION
Pittsburgh, Pennsylvania
For information
Andy Miller, MD '91
508-650-9181
andymerlier66@hotmail.com

MAY 18 AND 19
SCOPE AND SCALPEL
The Sixth Stench
Carlow College, 7 p.m.
For information
Ross H. Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

MAY 19
DEAN'S BREAKFAST MEETING
1105 Scalfe Hall, 9 a.m.
For information
Ross H. Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

MAY 19
CLASS OF '96 REUNION
Pittsburgh, Pennsylvania
For information
Marshal D. Peris, MD '96
mperis1988@aol.com

MAY 19
GATEWAY CLIPPER RIVER BELLE
CRUISE LUNCHEON
With Dixie Doc and the
Dixieland All-Stars
Pittsburgh, Pennsylvania
Board: 12:30 p.m.  Sail: 1-4 p.m.
For information
Ross H. Musgrave, MD '43
medalum@medschool.pitt.edu

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

OCTOBER 12
CLASS OF '41 REUNION
Pittsburgh, Pennsylvania
For information
Betty H. Bradley, MD '41
724-941-3715

OCTOBER 12 AND 13
PITT'S HOMECOMING AND
FAMILY WEEKEND
Pitt vs. Syracuse
Time TBA
For information
Ross H. Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

OCTOBER 12 AND 13
CLASS OF '76 REUNION
Pittsburgh, Pennsylvania
Mailing to follow

OCTOBER 12 AND 13
CLASS OF '81 REUNION
Pittsburgh, Pennsylvania
For information
Lydia E. Saris-Mechenbier, MD '81
412-563-0391
doclydia@aol.com

FALL 2001
CLASS OF '56 REUNION
For information
Robert Lee, MD '56
412-647-2758

FALL 2001
CLASS OF '46 REUNION
For information
Dwight Hanna, MD '46
412-826-5808

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

Although we have no doubt the cuisine at this year's senior class luncheon will be appetizing, the award-winning menu has nothing to do with food. Entrées will include tasty words of wisdom from, among others, this year's Hench and McEllroy Awards recipients. Afterwards, alumni, students, faculty, and other guests will adjourn to a Twentieth Century Club auditorium for the student awards presentation. This has the makings of a four-star experience.

For more information on the May 18 affair, contact the Medical Alumni Association: 412-648-9090. medalum@medschool.pitt.edu