“PLAIN PEOPLE,”
COMPLEX CURES

A BETTER LIFE FOR THEIR CHILDREN
SOMETIMES MEANS TRANSPLANTS
SOUTH BY SOUTHWEST

What could be better than the University of Pittsburgh Winter Academy in Naples, Fla.?

How about two winter academies? To reach even more alumni, we’ve added one in Phoenix, Ariz.

In only two years, the University of Pittsburgh Winter Academy has grown to become a premier event showcasing Pitt’s world leadership in research shaping tomorrow’s health care. Make plans now to attend—February 2008 in Naples or March 2008 in Phoenix.

For more information, please contact Pat Carver, director of alumni relations for the health sciences schools, at cpat@pitt.edu or 412-647-5307.

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

Pitt Med
400 Craig Hall
University of Pittsburgh
Pittsburgh, PA 15260
Phone: 412-624-4152
Fax: 412-624-1021
E-mail: medmag@pitt.edu
http://pittmed.health.pitt.edu

RECENT MAGAZINE HONORS
AAMC Publications Excellence

AAMC Robert G. Fenley Writing Award of Excellence
(C. Staresinic’s “Only Starzl Dared To”)

AAMC Robert G. Fenley Writing Award of Distinction
(J. Miksch’s “Hidden Connections”)

IABC Golden Triangle Award of Excellence
Book and Magazine Cover Design

IABC Golden Triangle Award of Honor
Magazine Design

IABC Golden Triangle Award of Honor
Feature Writing

CASE District II Accolades
Gold, Periodical Staff Writing
DEPARTMENTS

OF NOTE 3
Pancreatic cancer’s genetic helper.
Stress and a sweet tooth.
Rickets may be back.

CLOSER 7
At 17, it was about time she got a research gig at Cal Tech.

INVESTIGATIONS 8
Ubiquitin—it’s everywhere!
What do you feed trauma patients who can’t feed themselves?

MATCH RESULTS 33
Coming to a hospital near you.

ATTENDING 34
Science and murder.

ALUMNI NEWS 36
David Sherwood has seen some real cliffhangers.
A cancer drug that kills cancer too fast.

LAST CALL 40
Frankenstein’s 190th birthday.

FEATURES

“Plain People,” Complex Cures 12
The Amish and Mennonites are highly susceptible to inherited metabolic disorders. At the Clinic for Special Children near Lancaster, Pa., doctors refer all patients in need of curative transplants to Pitt.

COVER STORY/PHOTO-ESSAY BY CAMI MESA
TEXT BY JOE MIKSCH

The Modern Deathbed 18
The modern death ritual centers around the pounding of chests and other heroic measures. But that’s not what we say we want. Where do doctors fall short of offering “the good death”?

BY ELAINE VITONE

Defining Moments 24
Four Class of ’62 standouts look back on 45 years of discovery.

INTERVIEW BY SHARON TREGASKIS

Telltale Hearts, and Veins 28
Synthetic cardiac tissue is a design conundrum, but Pitt bioengineers are attracting attention with their prospective solutions.

BY MELINDA WENNER

CONTRIBUTORS

After high school, CAMI MESA (“Plain People,” Complex Cures*) was less than certain about her career path. A native of Colombia living in California, she enrolled in the Art Center College of Design in Pasadena, Calif., and picked up a camera and became enchanted: “I love to play with my composition, how it is working in the frame of my camera and how the lighting is hitting the subject. But more than anything, I try to find a connection between the person and myself.” Mesa says her trip to Amish Country for Pitt Med let her exercise what she calls her strength—portraiture. And she relished the human side of the assignment. “I wasn’t sure what to expect, but at the end of the day, all I could feel was an incredible community that comes together for each other,” she says.

MELINDA WENNER (“Telltale Hearts, and Veins”) is a Brooklyn-residing native of Denmark who earned a bachelor’s degree in music composition from the University of Michigan. With that diploma in hand, she embarked on a writing career and has since seen her work published in Scientific American Mind, SEED, The Boston Globe, and The Scientist. (Oh, she also has a bachelor’s degree in cell and molecular biology from Michigan and a master’s degree from New York University’s science, health, and environmental reporting program.) While working on “Telltale Hearts,” Wenner says she found herself moved by the patients’ stories: “[They] were inspiring. They have incredibly positive outlooks on life.”

COVER
Communities that normally eschew technology turn to transplants to cure their children.
(Cover: Cami Mesa © 2007.)
Beauty is unbearable, drives us to despair, offering us for a minute the glimpse of an eternity that we should like to stretch out over the whole of time.

—Albert Camus

In this issue of the magazine, a writer explores how physicians may fail to interact effectively with terminally ill patients and their families (“The Modern Deathbed,” p. 18). I know from my own experience as an oncologist how difficult it can be to relate squarely with families who are desperate for miracles. For instance, imagine how flummoxed a young doctor could become if a dying patient asked, “Just between you and me, Doc, we’re going to kick this thing, right?” So why don’t doctors handle these situations more skillfully?

The question makes me think of a talk Fadi Lakkis gave recently. Dr. Lakkis is the scientific director of the Thomas E. Starzl Transplantation Institute. He noted that, in the lab, sponges retrieved from the deep sea can be induced to fuse together into one organism if they are genetically identical. If they are genetically distinct, however, they repel one another (“innate immunity”). For 800 million years, this primitive ability to recognize “nonself” has been vital to the sponge’s self-preservation. The ability is critical to the most basic of biological needs—to reproduce one’s genes and thereby to sustain one’s “identity.” Fusing with another organism—even one of the same species—would permit the possibility that the organism might pass on the genes of another invading organism, diluting or even extinguishing the very identity that might otherwise offer a “glimpse of eternity.”

The immunology of sponges may seem leagues away from what takes place in our discussions in the ICU. Yet I submit that our instinct for preserving our identity is likewise conserved by millions of years of evolution. Moreover, as the renowned social anthropologist Ernest Becker has written, “the wellspring of all human activity is the fear of dying.” Absent our sense of these profundities, we cannot care for our patients with wisdom.

When we see our patients dying, we must confront our own mortality. At the National Cancer Institute, where I was an attending physician years ago, oncology fellows admitted, after some prodding, that they avoided their dying patients. Sometimes they unknowingly identified with them. Sometimes they were angry with them. The last thing young doctors wanted to do was to enter into meaningful discussions with terminally ill patients and their families that would stray from the reporting of medical facts—discussions that might touch on a parent’s guilt or a patient’s fear, for example.

But, as those oncology fellows learned, when physicians don’t run from their patients and instead come to see a patient’s experience as a guide to confronting their own mortality, the rewards are profound. We come to know our patients and ourselves at a deeper level, and we become better doctors.

Camus also said, “It is normal to give away a little of one’s life in order not to lose it all.”
Love in Springtime?

Pitt researchers have discovered that women who conceive in springtime are at a higher risk of delivering children prematurely. Women conceiving in summer have the lowest rate of preterm birth at 8.4 percent, with rates increasing steadily through the seasons and peaking in spring at 9.2 percent.

Lisa Bodnar and Hyagriv Simhan observed the spike when examining data from about 85,000 deliveries at Magee-Women’s Hospital of UPMC. Bodnar is a PhD assistant professor of epidemiology, of psychiatry, and of obstetrics, gynecology, and reproductive sciences. Simhan is an MD assistant professor of obstetrics, gynecology, and reproductive sciences.

The researchers say that the reasons for the spring spike are unknown but could be attributed to factors such as environmental allergens, dietary changes, and viral infections. Couples needn’t shy away from trying to conceive children in the spring, say Bodnar and Simhan. They see their study as a guidepost for future research into the roots of preterm birth, one of the most common complications of pregnancy. —Joe Miksch

FOOTNOTE

Stephen Esper (MD ’07) recently strutted about in a bathing suit and Godzilla mask, then stomped on a sand castle. Esper was named winner of this year’s inaugural Mr. Pitt Med pageant, a benefit for the Kenyan Pediatric HIV Project. The student’s angry lizard act (part of the swimsuit competition)—along with his fiddle performance and Chewbacca impression—netted him the title.

PANCREATIC CANCER’S GENETIC HELPER

The University of Pittsburgh’s David Whitcomb and a team of researchers are digging down to the root causes of pancreatic cancer, an aggressive and migratory killer. The group recently discovered a gene, palladin, linked to increased susceptibility for the form of the cancer that runs in families.

And by studying the genetic makeup of one family especially vulnerable to pancreatic cancer, Whitcomb has pinned down where the palladin mutation is located: chromosome 4q32-34.

Palladin is responsible for maintaining cell shape and function, says Whitcomb, an MD/PhD professor of medicine, of cell biology and physiology, and of human genetics. When palladin malfunctions, pancreatic cells morph. They behave like amoebas, as Whitcomb puts it, crawling away and allowing the cancer to spread rapidly.

These findings will help scientists develop a test to identify people likely to develop pancreatic cancer. Earlier detection will allow for earlier intervention in the form of laparoscopic surgery and other therapies. —JM
Observing the way a patient sits, talks, or stares is an important skill for a doctor. So how do you teach medical students to read other people? Maybe study a discipline whose practitioners look at people all day long.

That's exactly what Dean Arthur S. Levine (above) wants Pitt med students to do. He's the driving force behind a collaboration between the School of Medicine and The Carnegie Museums of Pittsburgh's art programs, including its Museum of Art, where Marilyn Russell (shown left) serves as curator of education, and The Andy Warhol Museum, where Jessica Gogan (shown right) is assistant director for education and interpretation. Students will study Carnegie collections to learn how artists see their subjects. It's an idea that has caught on at a few other medical schools as well.

On what doctors need to know that artists can teach them

Levine: When we see how a portrait artist visualizes another human being, we have a great deal to learn about diagnostic acuity. If I look at the portrait of King George by Velázquez or a portrait of the Madonna by Picasso, we begin to think about what the artist was seeing in that person, and what that person was feeling and thinking and perhaps articulating in ways that have common ground with how a patient and a physician interact.

How looking at art improves one’s ability to practice medicine

Russell: I think they're natural partners. Developing an interpretation of a work of art or finding personal meaning in it demands careful looking at exactly what the artist has provided. Viewers must consider not only the subject matter depicted, but even more importantly, subtle elements such as quality of brushstroke in a painting, body language and facial expression in figurative works, and the relationship and placement of objects within a composition. The context in which one experiences a work of art as well as prior knowledge can also affect what one takes away from the process of looking. It's easy to see how these would be important factors in the medical profession.

A question for us

Levine: Has a particular painting or artist caused you to view patients differently?

—Interview by Reid R. Frazier

Baca, a University of Pittsburgh MD/PhD student, isn't cruel; he just needs the tears to help develop a glucose sensor that could be placed inside a contact lens to monitor blood sugar in diabetic patients. When glucose levels rise, the crystalline structure of nanoparticles suspended in a gel swells, causing the gel to change color. If you were to see a small blue panel in your lens, then, Baca says, it might be time for insulin. Baca, Asher, and others recently published on the topic in the Journal of the American Society for Mass Spectrometry.

Baca finished his second year of medical school in 2003 and plans to have his MD degree in the bag in 2009. In the interim, he's been working on a Pitt PhD in chemistry. He has his eye on a career in emergency medicine.

Pitt geriatric psychiatry fellow Alexandre Dombrovski studies late-life depression, and his early work is making a mark. He recently won the American Association for Geriatric Psychiatry's Member-in-Training Research Award for a paper studying the efficacy of drugs and psychotherapy in elderly people who suffer from depression.

The study, to be published in the Journal of the American Geriatrics Society, found that depressed patients taking the antidepressant drug paroxetine reported better long-term social and emotional role functioning than those on placebo. The work was funded by the National Institute of Mental Health and the John A. Hartford Foundation.

Giorgio Raimondi won The Transplantation Society's research training fellowship—one of four research fellowships parceled out by the society in 2006. The PhD is a research associate in Professor Angus Thompson's lab at the Thomas E. Starzl Transplantation Institute. Working with mouse models, Raimondi tries to induce tolerance by isolating T-cells, treating them in vitro so that they recognize a transplanted organ as “self,” and reintroducing them into the mice.

“This area has been pretty hot for the past five years,” Raimondi said. “I really want to help create a robust state of tolerance, an acceptance of the organ” that would reduce or eliminate the need for immunosuppressive drugs. —JM
Sweats and Stress

A few years ago, the University of Pittsburgh's Janet Amico noticed how women she saw as patients were responding to stress and anxiety. She'd sometimes hear them talking about grabbing sweets or carbs to alleviate stress. Men, however, never seemed to talk about that.

Since then, Amico, an MD professor of medicine and of pharmaceutical sciences, and Regis Vollmer, a PhD professor of pharmaceutical sciences, have shown that oxytocin, a hormone associated with maternal bonding as well as dampening the blow of stress and anxiety, could have a role in keeping us from grabbing another slice of pie. The researchers monitored the feeding behaviors of a colony of normal mice and another of genetically engineered mice without the hormone. When the researchers augmented the animals' water with sugar, the oxytocin-deficient mice went on a binge, consuming four to five times as much water as they normally would. They also overdid it with carbohydrate-enriched water.

Amico and colleagues have also identified more anxiety and greater stress responses in female, but not male, oxytocin-deficient mice versus normal mice. She has broadened her studies to explore whether the enhanced consumption of sugar and carbohydrate solutions and greater responses to stress and anxiety are somehow related.

"It's still early to speculate," says Amico, about the hormone's role in humans, but the research suggests that some people's inability to say no to dessert could stem from an oxytocin problem. —Erica Lloyd

IS RICKETS ON ITS WAY BACK?

Rickets is usually associated with developing countries. In North America, first with the aid of cod liver oil supplements, then ultraviolet lamps and vitamin D–enriched milk, the bone-softening disease found in children was all but eradicated by the 1930s.

Kumaravel Rajakumar, assistant professor of pediatrics at Pitt, has found evidence that leads him to believe it might be on the rise here again. Half of the African American Pittsburgh-area children he studied (a sample of 42 between the ages of 6 and 10) were vitamin D deficient. If years go by without children getting enough of the vitamin, they can develop rickets.

"Rickets is back in North America in waves," Rajakumar says, even in sunny regions. Though rickets is not a disease physicians are required to report to health authorities, small studies like his own have brought Rajakumar to this conclusion.

“People with darker skin are more susceptible, needing up to six times the amount of sunlight required to generate an adequate supply of vitamin D in a light-skinned person. People in general aren't getting enough sunlight, mothers are depleted of vitamin D [through breast-feeding], and children don't get enough of it in breast milk and develop rickets," says Rajakumar.

Children and breast-feeding mothers should get more sunlight and consume more vitamin D–rich foods like fortified milk and other dairy products, he says. Vitamin D deficiency can also make one more susceptible to prostate cancer, multiple sclerosis, breast cancer, and diabetes.

Rajakumar received National Institutes of Health funding to monitor vitamin D levels in light- and dark-skinned children. —JM
Appointments

Thomas Gleason, an expert in aortic surgery, has joined Pitt. The cardiac surgeon's proficiency runs the gamut from the mending of aortic aneurysms to the repair of aortic and mitral valves.

Gleason, an MD, comes to Pitt from Northwestern University's Feinberg School of Medicine in Chicago. Here, he has become the director of the Center for Thoracic Aortic Disease at the UPMC Heart, Lung, and Esophageal Surgery Institute. He serves as associate professor of cardiac surgery in the School of Medicine.

In addition to assuming his surgical responsibilities, Gleason will oversee clinical and translational research aimed at treating those with thoracic, aortic, and valve-related diseases.

In many cases, asthma is a nuisance, making people reliant on inhalers or oral medication so that they can breathe freely. In other instances, asthma can be debilitating. New Pitt med recruit Sally Wenzel focuses on the latter cases.

Formerly a professor of medicine at the National Jewish Medical and Research Center at the University of Colorado Health Sciences Center in Denver, the MD plans to continue to develop treatments for severe asthma at Pitt. Here, she'll hold the positions of professor of medicine in the Pulmonary, Allergy, and Critical Care Division and director of its Asthma, Allergy, and Airway Research Center. Wenzel explores genetic factors contributing to severe asthma. She also hopes to further delineate the physiological differences that separate severe asthmatics from those with mild and moderate cases.

While at the Cleveland Clinic, obstetrician Stephen Emery was among the first to perform a procedure that used a needle and balloon catheter to penetrate a mother's uterus and restore blood flow in a fetal heart. Left untreated, the defect prevents organ growth and can necessitate a heart transplant. Since coming to Pitt, Emery has taught the technique to physicians here and says they are ready to perform it in Pittsburgh.

Emery joins the Pitt faculty after serving as cofounder and codirector of the Fetal Care Center at the Cleveland Clinic and assistant professor at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University.

At Pitt, Emery serves as assistant professor of obstetrics, gynecology, and reproductive sciences. He is pulling together a multidisciplinary team of surgeons, radiologists, and other specialists to join Magee-Womens Hospital of UPMC's Center for Fetal Medicine, which he leads. He plans to develop a comprehensive program for fetal intervention. —JM

EARLY SIGNS

As Robert Rogers sat on his porch preparing to give a class on saline lung flushing, his 11-year-old son approached him and asked:

“What are you doing?”
“Preparing a lecture on lung washing,” Rogers said.

The boy disappeared; a half-hour later, he handed his dad a drawing.

“My Dad The Lungwasher” (sic) was the first editorial cartoon by Robert “Rob” Rogers, on staff at the Pittsburgh Post-Gazette since 1993; his work is now syndicated nationwide.

When Rob Rogers started his professional cartooning career in 1984 at the Pittsburgh Press, his family often served as muse and model. In the meantime, his father, a Pitt professor of medicine since the early ‘80s, founded the department’s Pulmonary, Allergy, and Critical Care Division, as well as the clinical pulmonary physiology lab at UPMC Presbyterian. Artistry runs in the family: The elder Rogers paints. —Meghan Holohan
PRE PIT T MED

Alexis Chidi doesn't know if she wants to get her MD immediately or after earning a master's degree in public health. She's captivated by basic neuroscience, yet economics, French, and political science intrigue her as well.

As a University of Pittsburgh rising junior, the Rancho Palos Verdes, Calif., native has some time to make her decision. Chidi knows that if she finishes her undergrad years with a 3.7 GPA or higher and participates in appropriate medicine-related extracurricular activities, she's guaranteed admission to the School of Medicine. The “freshman guarantees” program attracts top high schoolers to Pitt by promising them a place in the University's graduate and professional schools. The program accepts about five pre-med students a year.

Chidi has a relaxed manner which belies her drive. After her freshman year at Pitt—she matriculated at 16—Chidi did a summer undergrad research fellowship at the California Institute of Technology, during which she studied language generation as it relates to defects of the corpus callosum, the structure that connects the brain's hemispheres. She developed and led the project and, as she says jokingly, “Got a team of grad students to push around.”

This summer, she may investigate stem cell research through a National Science Foundation program. Or, maybe, land a public health internship in Governor Arnold Schwarzenegger's office. Perhaps she'll work on a service-learning project in Tanzania. Or she might just take some more courses in organic chemistry.

Chidi says she'll figure it all out between classes, sorority soccer team games, and her duties related to serving in the student government, as vice president of her sorority, and on the Pitt Program Council.

—Joe Miksch
—Photo by Derek Wahila
After trauma, the body generates a frenzy of cells that produce the enzyme arginase, which shuts down the immune response. Oddly, these cells (shown with arrows) come from our immune system. The same thing seems to happen in certain cancers. Juan Ochoa believes understanding this mechanism will lead to life-saving diets for trauma patients and perhaps new cancer treatments.
Juan Ochoa started his doctoring career as a general practitioner with a bent toward preventative medicine in the 1980s. That was in the 8,000-foot-high mountain town of Santa Barbara, Colombia, a few hours’ drive from Medellín, where he’d spent his formative years. He even had a weekend radio show, “The Doctor at Your Home.” But Ochoa was fresh out of medical school, a bit naive, he says, and less effective than he expected to be. He would encourage women to breast-feed, for example, not realizing that practice was stigmatized in the rural area. Even the doctor on the radio wasn’t going to change people’s minds.

“I went there naively thinking I was going to be a missionary. And I left thinking, ‘This is far more complex than I ever thought.’”

Ochoa decided to specialize. Today, as a trauma surgeon and basic scientist, he is still a creature of prevention.

The questions the University of Pittsburgh professor of surgery and critical care medicine pursues now to save and improve lives are not so much about how to get people to change their behaviors, but how to convince cells to do so.

Since he first came to Pitt for clinical and research training in 1991, Ochoa has wondered: What do you feed trauma patients? Especially those who can’t feed themselves? Many surgeons wait a few days after surgery, until the bowels are functioning again, before feeding. Ochoa believed that the right diet, given earlier, would strengthen patients, helping them survive and stave off infection.

Studies have since suggested Ochoa was right. But feeding trauma patients is not a simple matter of inserting a tube and turning on a few monitors. The science behind nutrition after trauma is at least as complex as the social taboos of Santa Barbara. Our bodies are sometimes better able to cope with a little starvation than force-feeding, notes Ochoa. Trauma patients, in particular, are highly susceptible to infection. More than 50 percent with severe injuries are likely to end up with infections. And feeding someone the wrong formula can actually make it more likely the patient ends up on the unfortunate end of infections. And feeding someone the wrong formula can actually make it more likely the patient ends up with severe injuries are likely to end up with infections. More than 50 percent with severe injuries are likely to end up with infections. And feeding someone the wrong formula can actually make it more likely the patient ends up with severe injuries are likely to end up with infections. More than 50 percent with severe injuries are likely to end up with infections.

“Immune-enhancing” diet for surgical patients developed several years ago. That was on the heels of medical science’s realization that nitric oxide, the toxic gas your car coughs out of its exhaust pipe, is also manufactured by our bodies as part of the immune response. The diet includes, among other things, the amino acid arginine, a precursor to nitric oxide.

Ochoa believes the diet is probably appropriate for trauma patients and has tested safe for most other surgical patients. But surgeons aren’t in agreement about that. There’s no protocol in the United States—use of the diet differs from doctor to doctor and case to case. (The European society concerned with nutrition among surgical patients recommends using such diets before elective surgery.)

Now Ochoa believes that doctors are on the cusp of understanding how an arginine diet works and why it may be helpful for some patients and not others. His family ties have helped him make sense of the science.

His brother, Augusto Ochoa, is interim director of Louisiana State University’s Stanley S. Scott Cancer Center. When Augusto Ochoa was a researcher at the National Cancer Institute in the ’90s, he began to answer a question that perplexed many cancer researchers: Why don’t our immune systems put up a better fight against cancer cells?

“For many years,” Juan Ochoa explains, “doctors have been trying to boost the immune system to make it reject the tumor. But in a good number of patients, those lymphocytes that have been recruited to get rid of the tumor just don’t seem to work.”

In the early ’90s, cancer researchers, notably Augusto Ochoa, recognized that a peptide called the “zeta chain” was missing in lymphocytes (specifically T cells) of cancer patients.

“People didn’t know why it was lost, but they knew it was important,” says Juan Ochoa. T cells play a vital role in defending cells from viruses, foreign tissue, and other unwelcome guests.

Years later, in 2001, the Ochoa brothers began publishing reports showing that arginine was essential to maintaining the zeta chain. Around the same time, a Japanese scientist showed that trauma patients were missing the zeta chain.

Juan Ochoa had learned from his own investigations that arginase, an enzyme that metabolizes arginine, is present at elevated levels in the tissue of trauma patients. Patients with more arginase don’t do well. If they survive, they are sicker and stay in the hospital longer. The high levels of arginase somehow inhibit the ability of the injured body to keep the needed arginine in store.

The Ochoa brothers began exploring whether the immune system is dampened the same way in cancer patients. They found that arginase is elevated in the tissue of cancer patients, much like it is in trauma patients.

The brothers also learned what arginase was up to: At the heart of the immune response, it robs the arginine necessary to build the zeta chain. That leaves the T cell unable to proliferate to help fight off intruders and leaves the patient unprotected.

Augusto Ochoa and collaborators have since injected arginine into the tumor of a mouse. That therapy stopped the tumor from growing further.

Juan Ochoa believes that immune-enhancing diets work similarly: A high concentration of arginine restores the zeta chain, allowing the T cell to do its job to fight off infection.

“It’s not proven. But we’re closing the loop on that,” he says.

He’s anxious to start refining a diet for precommercial testing in trauma patients. (Arginine, for example, doesn’t taste great and can have adverse effects. Juan Ochoa is looking toward substituting it with citrulline, a more palatable amino acid found abundantly in watermelon. Citrulline works the same way and seems to be safer.) “Now that we know the mechanism, we can make better diets,” he says.

He’s optimistic about the possibilities: “So if we could block the [process that cuts out the zeta chain], we could potentially have a treatment for cancer. We could also have a potential treatment for infection in trauma.”

He suspects that the immune system is dampened the same way in leprosy and tuberculosis and wonders whether those diseases could be managed through diet as well.

Jessica Mesman contributed to this article.
In the 1970s, American researchers were looking for clues to the cause of the human autoimmune disease myasthenia gravis. They found a protein that appeared to have some of the properties that could make it a potential cause of MG. When researchers added the protein to certain types of human immune cells, those cells became more specialized. Investigators also were intrigued by the fact the protein was very good at attaching itself to other proteins, suggesting it had some immune properties.

Unfortunately, their candidate protein flunked the final, and most crucial, test. Researchers believed that for the protein to be involved in MG, it needed to be unique to the thymus gland, which is where immune cells get their marching orders. But when they looked for the protein in other kinds of cow tissue, the medium of their first
was using the energy—figuring it was chewing consumption of energy. Looking for what released inside cells, there was a corresponding phenomenon known as “energy dependent protein degradation.”

Ubiquitin would not resurface as a research topic until five years later when two Israeli scientists, collaborating with an investigator at the University of California, Irvine, set out to find the explanation for a recently discovered finding in pigs, guinea pigs, mice, plants, insects, people, even yeast. The only place it didn’t show up was in a few primitive microorganisms. In 1974, the scientists introduced their new protein—aptly named “ubiquitous immunopoeitic polypeptide” (later shorthand to “ubiquitin”)—in a paper in the Proceedings of the National Academy of Sciences. Then they promptly abandoned it because it wasn’t the thymic hormone they sought. An aside at the end of the PNAS paper noted that the protein occurs so universally it must be an “integral feature” of nearly all living things.

Researchers in the 1970s had noted that whenever there was a burst of amino acids released inside cells, there was a corresponding consumption of energy. Looking for what was using the energy—figuring it was chewing up proteins and releasing amino acids in the process—the investigators turned up what they thought was a newly discovered protein. It seemed to be able to degrade other proteins under certain conditions. Upon talking to their colleagues and searching the scientific literature, they realized what they’d come upon was ubiquitin.

In a flurry of studies in the early 1980s, researchers showed that ubiquitin does not degrade proteins directly but rather flags them for demolition by a long, hollow molecule called a proteosome. It takes at least four ubiquitin tags for a protein to be targeted for destruction. As the protein is degraded by the proteosome, the ubiquitin molecules are liberated, free to search out potential new target proteins for disposal.

And scientists made another important discovery: Ubiquitin mostly tags abnormal proteins for destruction. Unfortunately, it took a few decades before the full implication of this latter finding was appreciated. As one retelling of those events recently noted, ubiquitin research “was little more than a backwater of biochemistry studied by a handful of laboratories” for many years to come.

Ubiquitin’s status as a topic of research interest did not change dramatically until 2003, when the Israelis and one of their American collaborators were given the Lasker Award for their work on the ubiquitin-proteosome pathway. A year later, the two Israelis and another American colleague were awarded the Nobel Prize for Chemistry.

Scientists now recognize ubiquitin as a master regulator of a broad host of cellular processes. They suspect that alterations in the ubiquitin-proteosome protein-disposal system factor into a number of diseases, including neurological conditions, liver diseases, eye diseases, and a variety of cancers.

Just as the greater scientific community was beginning to recognize the importance of the ubiquitin-proteosome pathway, Yong Wan, now a PhD assistant professor of cell biology and physiology at the University of Pittsburgh School of Medicine, was arriving at Pitt after completing his postdoctoral training at Harvard University.

At Harvard, Wan had worked for cell biologist Marc Kirschner. One of the first to understand the importance of the pathway for normal cell functions in the mid-1990s, Kirschner and his lab had discovered a ubiquitin ligase known as anaphase-promoting complex (APC), which is involved in making sure that cells divide properly. Kirschner assigned Wan to work on APC, and Wan brought that project with him to Pitt in 2003, where he was one of just a handful of investigators (including the medical school’s dean, Arthur S. Levine) interested in this relatively new area of inquiry.

Today, Wan’s lab is one of several dozen at Pitt delving into aspect of this multifaceted enzyme. Others are investigating ubiquitin’s role in neurological conditions, including Alzheimer’s, as well as xeroderma pigmentosa, an inherited disease that makes people extremely sensitive to natural sunlight while putting them at high risk for skin cancer. The disease can inhibit the effects of radiation therapy and chemotherapy on tumors, promote the growth and proliferation of cancers, and influence circadian rhythms.

Wan has several large grants from the National Cancer Institute and the American Cancer Society to not only investigate APC’s role in normal cell division but also to look at whether environmental factors, such as chemicals or radiation, might damage APC or cause other alterations in its activity.

“The major role of APC is to control the separation of chromosomes during cell division by ungluing the chromosome strands. Deregluation of this separation process usually results in catastrophic alterations in the shape and number of chromosomes in a cell, which is a hallmark for many types of tumor cells,” Wan explains.

His laboratory, based at the University of Pittsburgh Cancer Institute, also looks into ubiquitin’s role in stem cell maturation. Wan believes the ubiquitin-proteosome system acts like a licensing agency, allowing stem cells to become specific types of cells, such as muscle or liver cells, by orchestrating the degradation of all but one type of signal.

Others at Pitt have suggested that ubiquitin influences how we perceive the world.

The laboratory of Yong Tae Kwon, a PhD assistant professor in the Center for Pharmacogenetics in the School of Pharmacy, explores a pathway in the ubiquitin-proteosome system called the N-end rule pathway.

Wan believes the system acts like a licensing agency, allowing stem cells to become specific types of cells.
In a parking lot populated by a dozen or so hundreds-of-horsepower cars and SUVs also sit a couple of one-horsepower conveyances: Amish buggies. This is the Clinic for Special Children in Strasburg, Pa. Amish and Mennonite men constructed the clinic here in 1991 and expanded it in 2001.

On the front porch, a docile black dog named Bowie greets patients and visitors. Inside are women wearing unadorned clothes and bonnets. (The Amish, Mennonites, and others who settled the area in the 1700s in search of a humble life and religious freedom often call themselves “the Plain People.”) Children play in the waiting room. One child roots through a toy chest full of Beanie Babies. Sunlight streams into the building from 78 windows. Down a hallway where skylights brighten the oak floor and fir beams (held together with wooden pegs rather than nails, the custom for Amish and Mennonite construction), and past a genetics lab, a family sits in an alcove in close conversation with physician Kevin Strauss.

The family is Mennonite. They are from southern Alabama, not far from the Florida panhandle. Their baby daughter is squirming on her thin father’s lap. The girl has a rare genetic condition called maple syrup urine disease (MSUD). It is more common by orders of magnitude among Amish and Mennonites—the ratio is one in three-hundred for them and perhaps as high as one in a million for the population at large, says Strauss. MSUD, which gets its name from the sweet smell of the afflicted child’s urine, is a metabolic disease that causes amino acids to accumulate in the body. It can lead to brain swelling, neurological damage, and death. The only cure is liver transplantation. Although MSUD is not a liver problem per se, a new liver compensates for the lack of critical enzymes normally found throughout the body. Almost immediately after transplantation, an MSUD patient’s metabolic health reverts to normal.

The Clinic for Special Children, cofounded by West Virginia native and Harvard-trained physician Holmes Morton and his wife, Caroline Morton, is one of the best places to get diagnosis and treatment for genetic disorders particular to the Amish and Mennonites, including MSUD. Children’s Hospital of Pittsburgh of UPMC has become the clinic’s go-to hospital for the curative transplant.
Of course, transplantation has its risks. In addition to challenges presented by the surgery itself, patients must perpetually take immunosuppressants. Yet Pittsburgh boasts an overall survival rate among pediatric patients of 83 percent 10 years after a liver transplant. And all 38 of the Clinic for Special Children’s patients transplanted at Children’s—28 because of MSUD—are thriving.

The Alabama family has come to the clinic to find out for themselves about the benefits and pitfalls of transplantation. The young father (the family asked that their names not be used), dressed in black trousers and a white button-down shirt with a cell phone hanging from his belt, says to Strauss, “My opinion was [the Mennonite community] doesn’t do transplants.” That was, he adds, until a member of a Mennonite family close to his did.

The father came prepared with a list of questions regarding mortality on the operating table, immunosuppression, rejection, maintenance of MSUD through diet, and cost. (Mennonites and the Amish typically do not carry health insurance. It’s a pay-as-you-go process for them, with material help given by friends, family, and other members of the community. The cost of a liver transplant, Strauss says, is equivalent to about a decade of typical treatment, and treatment can go on for 30 or 40 years or longer.)

As the father talks, a toy placed next to the band of preschoolers sitting on the floor erupts into a rousing rendition of “London Bridge.” Amid the commotion, Strauss does his best to allay the man’s fears.

“One thing we can tell you—one thing we are obligated to tell you—is that [transplantation] cures MSUD in every case and cures it 100 percent,” Strauss says. “There’s no longer a need for a special diet, there’s no need for blood testing. That’s it.”

What that means, Strauss tells the father, is normalcy. There will be no metabolic crisis, no dietary restrictions (MSUD patients have to carry a special dietary protein powder with them at all times), and no risk of MSUD-related brain damage or death. There can and likely will be medical problems related to the transplant, he says, but “it’s a good trade-off.” To reap these benefits, Strauss continues, leaning forward. “You have to go where they know what they’re doing. That’s Pittsburgh. You have to go to Pittsburgh. We’re partners. They can manage any crisis.”

The clinic’s relationship with Pitt has taken root throughout the past three years under the direction of George Mazariegos (Fel ’93), an MD associate professor of surgery at Pitt and director of Pediatric Transplantation at Children’s. Morton and Strauss worked with him—along with colleagues such as Jerry Vockley, MD/PhD chief of the Division of Medical Genetics at Children’s and professor of pediatrics and human genetics at Pitt, and David Finegold, an MD professor of pediatrics, medicine, and human genetics at Pitt—to develop transplant protocols to deal with and stave off the metabolic crises potentially faced by MSUD sufferers.

Strauss acknowledges there is resistance to transplantation in certain segments of the Mennonite and Amish communities, particularly those near the clinic.

“From the beginning, there’s been opposition. People have felt that Dr. Morton and the clinic are right here and can manage MSUD. But Dr. Morton and I both know we can’t fully protect anyone from the risks of MSUD,” Strauss tells the family.

The father turns to his wife, then looks back to Strauss and says, “We’re going to go home and think.”
Dustin Hahn and his parents, Dawn and Kevin Hahn, have already made their decision. Dustin will have his transplant. A cheery homeschooled seventh-grader from Lititz, Pa., who's quite comfortable in the presence of adults (perhaps from a lifetime of dealing with doctors), Dustin came to the conclusion he was ready as the 2006–2007 ice hockey season approached.

“He asked Dr. Strauss if he could play on a hockey team,” Dawn Hahn says. She reports that Strauss said Dustin could, but it would mean a lot more work to keep him healthy, because soft bones are a consequence of MSUD.

As the Hahns discuss Dustin's potential hockey career (he's a Philadelphia Flyers fan), Strauss joins them in the waiting room. Picking up on the conversation, Strauss says, “Hockey for [Dustin] is just the tip of the iceberg. There are benefits in terms of attention and education and employment. Adults with MSUD don’t take as good care of themselves as their parents did when they were children. There are mood disorders to consider. About 30 percent of adults with MSUD are on antidepressants—that’s three or four times higher than the general population.”

Dustin has been on the liver transplant waiting list since January. Since then, Children’s has called twice telling the Hahns a liver was available, but both times they got a follow-up call before they could make the four-hour drive to Pittsburgh. The organs were not suitable for transplant, they were told.

“I was excited,” Dustin says, “and a little scared. My heart went down when we found out it wasn’t going to work, but I got over it. It’s practice.”

“We don’t want a lot more practice,” his mother chimes in.

So Dustin waits for his opportunity to eat “regular” food (he wants a bacon cheeseburger and a Frosty from Wendy’s), play sports, and be able to concentrate better in school. He is hopeful, and, in fact, his greatest fear seems to be that the doctors and nurses at Children’s will try to turn him into a Pittsburgh Penguins fan. “Flyers all the way,” he says.

Dustin Hahn received his transplant shortly before Pitt Med went to press.
Statistically speaking, most of us will die like Gene Smith is now—lying in a hospital bed amid the rhythmic chirping of machines. He has a life-limiting, chronic illness—one of the usual suspects that kill Americans—and has been seeing a specialist for some time. At his last appointment, he got the news: Treatment isn’t helping anymore.

Smith’s nursing home transferred him here last night when he began having trouble breathing, which the hospital staff says may or may not be due to his chronic illness. Now his blood pressure is dangerously low. He gasps inside his facemask, though it’s putting concentrated oxygen in his lungs. His wife, Nancy Smith, holds his hand.

Hospitalist Jane Miller walks in and introduces herself. “I’m sorry to be meeting you under these circumstances,” she says, standing beside the bed. “So, what’s been going on?” Her eyes bow with concern. From reading his chart earlier, she knows—as the Smiths do—that Smith has only a few months, at best. At worst, he will die much earlier—certainly within 24 hours if he isn’t put on a respirator soon.

Where do we fall short of providing “the good death,” and what can we do to improve?

ILLUSTRATIONS | CATHERINE LAZURE
Studies show that doctors tend to paint a brighter picture to patients and their families than the doctors themselves perceive.
that some schools offered no training in end-of-life situations at all. New doctors might be a little better prepared. In 2003, a study reported that 60 percent of fourth-year students surveyed had been trained to discuss treatment withdrawal with patients or their families. Yet 82 percent of students and residents said they’d taken no courses in end-of-life care. A recent survey found only about 5 percent of practicing oncologists have had any form of communication training. All too often, doctors are ill prepared for the needs of dying patients and their families.

Though the details vary, research shows that dying patients consistently describe the same desires: They want to manage their pain and symptoms, feel a sense of preparedness and completion, be valued as a whole person, and remain clearheaded and able to make decisions for themselves. Without clear communication between doctor and patient, all of the above can be difficult.

Although Barnato empathizes with her study’s participants, it worries her that their decisions regarding Smith’s treatment have been “all over the map,” from intubation in the ICU all the way over to what Smith actually wants: palliative care, a subspecialty focused on providing comfort, dignity, and control to patients with life-limiting illnesses. However, the actors are trained not to ask for it. “Even in a simplified case in which the simulated patient has underlying goals and preferences that are scripted and waiting to be unearthed,” says Barnato, “the patient’s treatment plan is at the whim of the physician.”

Barnato says that for the doctors participating in the study, it’s all a matter of perspective. Do they see the big picture or the immediate problem—the forest or the trees? If they are focused on the trees, they’re looking at the numbers, adjusting Smith’s oxygen, concentrating on getting him through the next 24 hours. If they see the forest, they recognize that there is much more at stake, and now is the time to address his wishes directly. The longer this discussion is put off, skirted, or derailed by talk of vitals and treatment options, the less likely it is that Smith will die the way he wants to.

Palliative care began in the United States in 1974, when the country’s first hospice was founded (the Connecticut Hospice). However, it only became formally recognized as a subspecialty in October 2006. In 2005, the American Heart Association included palliative care recommendations in its guide-
lines for the first time in the organization’s history.

At the state level, a new Pennsylvania law covering decision-making procedures for terminally ill patients took effect this February. Incidentally, that was just days before Governor Ed Rendell’s administration released a 40-page report of recommendations for improving end-of-life care. The document’s 160 recommendations aim to improve research, outreach, advance-directives policy, healthcare-finance structures, professional education, sensitivity to the needs of special populations, and palliative care standards—especially in acute-care hospitals, where most Pennsylvanians die.

On February 9, scholars from around the world gathered on Pitt’s campus for a seminar on end-of-life issues, hosted by Pitt’s Cultural Studies Program and School of Medicine. The springboard for the discussion was The Contemporary Deathbed, a book by emergency-medicine specialist and cultural historian John Tercier of the University of California, San Francisco. The book focused on the iconic image of death in the media—the heroic CPR attempt that often takes place after a patient’s last breath. Tercier questions why CPR has been so central to resuscitative procedures across a gamut of cases, even though it has been proven effective only when administered immediately after certain types of cardiac arrest. “For a number of years now,” he writes, “medical personnel, while pumping on the chests of the dying, have been asking themselves, ‘Why are we beating a dead horse?’”

Perhaps the question now is: How do we stop?

It’s not news that few Americans want to end their time on earth in a hospital, with intensive—not to mention expensive—life-sustaining treatment. Yet that’s exactly what most get. In the last three decades, 27 percent of the total Medicare budget has been spent on treatment during Americans’ last year of life and, of that, about 40 percent in the last month.

Given that so many doctors are uncomfortable even asking patients about their wishes, it’s not surprising that the contemporary deathbed still has more than a few bugs. For all our dollars spent and efforts made, and all our talk of living wills and other advance directives, we’re often still missing the mark. Where do we fall short of providing the good death, and what can we do to improve? Barnato and others at Pitt are starting to answer these questions.

Pitt’s Bob Arnold, a former president of the American Academy of Hospice and Palliative Medicine, says the good death has remained elusive for a variety of reasons. To name a few: Patients and families don’t know to expect good palliative care, healthcare providers haven’t traditionally been trained to provide it, and health care in this country is financed with an emphasis on acute rather than chronic illness.

To address these issues, Family Hospice and Palliative Care—one of the first hospice programs in Pennsylvania—and Pitt’s health sciences schools jointly established the Institute to Enhance Palliative Care in 2003. The institute educates healthcare providers about palliative care, raises public awareness about palliative care availability, advances public policy supporting better care for seriously ill patients, and conducts research into best practices.

“Twenty or 30 years ago there would have been no one looking at this stuff,” says Arnold. “Now there’s a whole group of junior investigators and researchers at Pitt who are all really interested in focusing on these issues.”

David Barnard, who directs the Institute to Enhance Palliative Care and palliative care education at Pitt’s Center for Bioethics and Health Law, says one of the bigger problems with the contemporary deathbed is the way prognosis is often communicated. Studies show that doctors tend to paint a brighter picture to patients and their families than the doctors themselves perceive—either consciously because they’re uncomfortable or unconsciously because the better doctors know their patients, the more likely they are to be overly optimistic in their predictions. This leads to problems once a patient really starts to decline.

As a member of the UPMC Ethics Committee, Barnard has seen it countless times: The patient has multisystem failure and has been on a ventilator for two weeks, failing 10 years after the surgery.

The doctor calls and says, “The family doesn’t get it.” Barnard explains: “Too much time is spent deciding which treatments to do, rather than getting to know the patients and what they want. The important question they should be asking patients is: ‘What characteristics of life make it worth living?’”

In 2001 and 2005, Barnard secured four-year National Cancer Institute (NCI) grants—totaling about $1.75 million—to incorporate new palliative care offerings into the curriculum. Palliative care training is now available at all levels of instruction, from classroom to residency to fellowship.

In one course, Barnard pairs first-year students with patients with life-threatening illnesses. They spend time together throughout the semester. Medical student Yohko Shinozawa (Class of ’08), who took the class two years ago, was assigned Mike Kolansky (not his real name), a bearded, tattoo-clad motorcycle enthusiast in his 60s. Kolansky had undergone a liver transplant, and, as a result of his immunosuppressant medications, his kidneys began

“Medical personnel, while pumping on the chests of the dying, have been asking themselves, ‘Why are we beating a dead horse?’”

Each Saturday, Shinozawa sat with him for one hour of his 12-hour weekly dialysis regimen at the VA hospital.

To Shinozawa’s surprise, the two didn’t discuss his illness much. “He was laid-back, always joking around,” she says. “He was very focused on living and making the most of his life.” Since her semester in Barnard’s class, she has volunteered regularly for the palliative care program.

The institute also offers a two-year palliative care fellowship that combines research with clinical care. First-year fellow Elizabeth Weinstein (MD ’02, Res ’05) notes that while many palliative care fellowship programs are run through oncology or geriatrics divisions, Pitt’s is part of the Division of General Internal Medicine. “One of the things I love about Pitt is that we see such a broad range of patients.”

Weinstein says that a feather in the program’s cap is Arnold himself. “A couple of weeks ago we were at a national meeting. Everyone was grabbing for five minutes of Bob Arnold’s time. ... But he always down-
plays what he does. You wouldn't realize he's one of the heads of this new field."

Arnold worked with colleagues at the University of Washington, Seattle, to create Oncotalk, a four-day retreat funded by the NCI to train oncology fellows in communication skills. (Oncotalk was featured in *The New York Times* in January.) In spring 2008, Arnold will begin a new retreat, funded by the Jewish Healthcare Foundation of Pittsburgh, to train pulmonary and critical care fellows to conduct family meetings.

Arnold says facilitating conversations with groups of people in the middle of a highly emotional situation is an acquired skill. "You have to practice... Often people will focus more on the cognitive material rather than the emotional."

Barnato, who interned in general surgery before pursuing her career in research, can relate. "We'd tell you about every aspect of your mom's physiology, every organ system, and then we'd just end with a 'We're doing everything we can.' That was our form of a family meeting."

One case from her internship working in an ICU in another state stays with her. It reminds her how patients and their families can be cut out of the decision-making process. After inserting bilateral chest tubes—an aggressive surgical measure known to help in some cases of respiratory arrest—Barnato was able to bring an 85-year-old woman back from a code blue. The patient was then transferred to a long-term, acute-care facility, where she died a few months later.

"We had amputated her feet and parts of her lower legs," says Barnato. "She was bed bound and on a ventilator. Her favorite thing to do was watch TV, and she wasn't going to be able to do that because she was now almost blind because of her diabetes."

While the patient awaited her transfer, Barnato approached her and asked about her wishes. Though she couldn't speak, through notes and gestures the patient told Barnato that this wasn't what she wanted.

Barnato was nervous about bringing it up but ultimately decided she had to. "Do you know what my resident did?" she says. "He ordered a psychiatry consult. The psychiatrist came, saw her, and decided she was depressed. And he started her on—I'm not kidding—Prozac. ... It was very demoralizing, to say the least."

In a study published in *Critical Care Medicine* in 2004, Barnato looked at the final hospitalizations of deceased patients across the country, comparing the aggressiveness of treatment. She found that in some geographic regions, the average ICU stay was much longer than others. Since then, she's found a lot of variation from hospital to hospital, ICU to ICU, and doctor to doctor. Recently, she interviewed staff members at 11 Pennsylvania hospitals, asking them about end-of-life decision-making. She heard statements like, "This doctor tends to do this, but that doctor tends to do that"—unsettling for Barnato. "You’d hope these decisions would be made by the patient and the family [rather than the doctor alone]," she says.

A few hours after Miller's simulation, Arnold enters Smith's room, introduces himself, and squats beside the bed so that he's almost looking up at Smith. If this were more than role-playing, he would have roamed the halls looking for a chair—meeting the patient at eye level is that important.

Through a series of open-ended questions, Arnold gets the couple talking. They tell him all they know, including what's going on with the chronic illness they've been fighting all these months.

Arnold repeats it all back to them. "And so some of this may be because of [the illness]. Or it could be pneumonia. Or it could be a blood clot. And the problem right now is it looks like he's gotten a fair amount worse, and it could be because of any of those things. And I guess the question is, Where do we go from here?" He pauses, then begins again, his pitch higher, his timbre softer. "After you found out that [the illness] was worse, had you guys ever talked about where you'd go?"

They explain that they have a living will at home that says Smith "doesn't want anything extraordinary."

Arnold clarifies that they all agree on what extraordinary means.

Then he addresses Smith directly, asking him if anything besides the shortness of breath is making him uncomfortable, what his wishes are, and whether or not he wants to be part of the conversation in the first place. "Some people when they're sick don't want to hear a lot about the medical details," he says, "and other people want to hear what's going on."

He suggests medication that will ease Smith's discomfort. He turns off the noisy machines that distract the couple from each other, assuring them that Smith is still getting his oxygen. He asks if any loved ones or clergy need to be there, and what kind of support Nancy Smith has. Again and again, he asks them, "Questions?"

Arnold is a palliative care specialist who helped design this study, so he knows exactly what to do in this simulation. Still, listening to him is inspiring—a reminder of what's possible as American doctors become comfortable adding palliative care to their broader definition of healing.

For Shinozawa, the definition of the good death has become more nuanced as she volunteers for Pitt's palliative care program.

Some patients want somebody to talk to. Some like the silence but still want companionship. Some can't tell you what they want, because they're unable to speak or write, and it takes a lot of yes-or-no questions to understand their desires.

And then there are the patients who simply want to focus on living with an illness—like Kolansky the biker. "Don't take life so seriously," he told Shinozawa the day they met. "Take it as it comes."

Once, she asked, "Is there any one thing you want to do before you die?"

"Go on one last ride," he said. He added that he didn't want to burden his family with a funeral. "Sprinkle my ashes on my Harley," he said, joking. "Take me cruising one more time."

"Death isn't easy to talk about," says Shinozawa. "It's not like after we take this course we become experts on this. But I think it's a good start."
The University of Pittsburgh medical school’s Class of ’62 trained in the shadow of giants—biochemist Klaus Hofmann, pathologist Frank Dixon, internist Jack Myers, Jonas Salk and Julius Youngner of the killed-virus polio vaccine, surgeons Henry Bahnson and Albert Ferguson. Molecular biology was an emerging field, and even first-year students could contribute to the explosion of knowledge. Nearly half a century after they earned their degrees, four members of the Class of ’62 recall moments that shaped their careers and reflect on the life of the physician-scientist, a profession some have called endangered.

Brooklyn’s SUNY Downstate Medical Center professor of medicine Albert Braverman, a hematologist-oncologist, has investigated breast cancer treatment, thalassemia, and sickle-cell disease. Braverman’s credits include medical publications as well as literary analyses of the works of Thomas Mann and Robert Frost. Director emeritus of the renal division at Brigham and Women’s Hospital Barry Brenner is the Samuel A. Levine Professor of Medicine at Harvard University. He authored the textbook *The Kidney* and defined the role of the glomerulus in chronic...
renal diseases. John Hibbs is Distinguished Professor of Internal Medicine and chief of the Division of Infectious Diseases at the University of Utah in Salt Lake City, where former classmate James Kushner is the M.M. Wintrobe Distinguished Professor of Internal Medicine and heads the Division of Hematology. Hibbs garnered a Nobel Prize nomination for teasing out the biochemistry of nitric oxide. Kushner serves as director of the University of Utah’s Center of Excellence in Molecular Hematology; he delves into genetic disorders of iron metabolism.

These far-flung old friends gathered this winter through teleconferences. Here we share excerpts of two recent conversations.

PM: What do you remember of one another as students?

Kushner: My most striking memory of Albert Braverman involves incredible glassware breakage during biochemistry lab. He smoked Turkish cigarettes.

Braverman: Gauloise. My wife is Turkish, but I don’t smoke anymore.

Brenner: Albert and I were in adjacent rooms on the eighth floor of Salk Hall. Having him as a next-door neighbor was one of the great enrichments of my young life. He carried an aura of goodwill that spread to everyone he met and touched.

Hibbs: We would often eat together in the cafeteria at Scaife Hall and have these wonderful, free-ranging discussions, always intellectual.

Brenner: On Friday nights, we’d go down to Canton’s in Oakland. It was $2.95 a dinner. Not much wine was poured, but they did have wonderful food. Those dinners were probably three hours.

Braverman: I came to medical school interested in psychiatry. Because of Barry, my interest turned to science. He was the first person I knew personally who had an intellectual interest in science and clinical medicine. John had intelligence, breadth, moral rectitude, seriousness, and good humor. It was a tremendously enriching time.

Brenner: John was tall, very handsome, casual in appearance. Never the type to interrupt, he’d just let you talk and then he’d respond. Jim was very smart, witty. Pitt was my first away-from-home experience. Right from the start, Jim, you were in an apartment.

Kushner: I lived on the second floor of a funeral parlor on Negley Avenue. In the evening, I and my roommate—Eduardo Delgado (MD ’60)—would cruise through the salons and, instead of supper, eat all the chocolates that were set out for the mourners.

Brenner: But did you have any embalming responsibilities?

Kushner: Barry, I remember you were very funny, with round glasses and an ability to incorporate knowledge at a tremendous pace. Medical school seemed very easy for you.

Brenner: I spent that whole summer before medical school working in the post office. The foreman told me, “You better do well in medical school because you wouldn’t have any future here.” I was motivated, having been cut off from this other opportunity.

Braverman: I was a very successful message runner on Wall Street. That career was open to me.

Kushner: Barry, you were commenting that John was a casual guy. John is a hopeless romantic. He sees drama and romance everywhere, particularly in science. I remember when he was first discovering the pathway from L-arginine to L-citrulline and nitric oxide, and how macrophages got activated. It was like listening to the most wild-eyed guy in Union Square standing on a soapbox.

Braverman: I remember John’s macrophage paper. I had my doubts about the immunotherapy of cancer, and here I saw this paper in Science—and from macrophages and cancer came an overwhelmingly important discovery [the mechanism for formation of nitric oxide in the human body] that was completely separate.

Brenner: John should have received the Nobel.

Kushner: He couldn’t. He doesn’t have a tie.

Brenner: I would not have guessed, from the four years we were in medical school, that John Hibbs was destined for a career in basic science. John, tell me why I missed it.

Hibbs: When I was in medical school, I didn’t do any science other than our laboratories—biochemistry, physiology, etc.—the smells and the activity seemed far removed from clinical medicine and what we were learning from the textbooks and professors.

Braverman: When did it change for you?

Hibbs: Jim and I were both drafted when we were interns. There was a hemorrhagic fever epidemic that began in eastern Bolivia, and I volunteered to go down and work with some scientists from the NIH. It was physical adventure, but the research turned out to be intellectual adventure.

There’s nothing more stimulating than working in a basic research laboratory, once you learn how to use the scientific method. It’s so powerful, so basic, and it’s the rigorous testing of knowledge that separates science from superstition, from ideology, theology. It doesn’t produce absolute truth, but it gets us closer. There’s so much excitement in seeing things for the first time.

Kushner: See what I mean about him being a romantic? I found my transforming event in the pathology laboratory experience with Frank Dixon [the pathologist who showed that the immune response could cause disease].

Brenner: One of my interviewers was [molecular biochemist] Harold Segal. Not only did he set in motion my acceptance letter, but with it came an invitation to start work in his laboratory on the day I started medical school. I sent off a manuscript in January of my first year. It has my name as B. Morton Brenner. I went through this affectation that lasted only as long as that paper. Someone said to me, “Oh my god. I’ve been calling you Barry. I should call you Morton.” I said, “Never mind, I’ll change my name back.”

PM: What was Pitt like then?

Braverman: This was the decade in which molecular biology came into being. The microbiology course was where we heard about tRNA and mRNA and all the things that were coming out then, where we got the foundation.

Brenner: I think it was the virology component, Al. Julius Youngner was giving these lectures where it was as if he would read a paper and the following week, the material was incorporated into the lecture. There was almost no dwell time.

We got to do that serum sickness experiment under [pathologist] Joseph Feldman’s guidance.

Braverman: Low titer, medium titer, high titer. Medium titer did it.

Hibbs: The School of Medicine had gathered together a unique group of human beings both in basic science and the clinical years. It was like Athens during its heyday or Florence during the Renaissance.

Braverman: One person was more unique than the others. [Department of Medicine chair] Jack Myers was a force in Jim Kushner, I can attest to that.

Kushner: As a physician, a clinician, everything about me—my whole personality—was transformed by him. He knew his own mind. He had the courage to think through a clinical situation. And he really believed that doctors had to take responsibility to do things that were difficult.

Brenner: I remember presenting to Jack at the bedside, at 10 o’clock in the morning. You worked up the patient the night before, finished around midnight, stayed in that little Presbyterian Hospital library, read everything you could about the diagnosis you were entertaining. This year, on my first day of general medicine, I had a kid...
“It was like Athens during its heyday or Florence during the Renaissance.”

Tell me about one of his 22 admissions the night before, but he had a clipboard in front of him. He’s reading to me the age, the name, the history of the present illness. I said after 12 seconds, “Put your notes down. Just tell me about the case.” He couldn’t. I said, “We will have no more rounds today. Tomorrow, whoever presents better know the case, not the notes. Show me that there’s been some integration of the information.” I was brought before the department chairman as being out of line.

Kushner: That was Jack Myers speaking through Barry Brenner.

PM: What else stood out?

Brenner: The attendings we had were chiefs of service. Today the attendings—I only know it from where I work—are people who are out of their training a year or two, or they’re hospitalists.

Braverman: I had [as attendings] Gerry Rodman, head of rheumatology; Abe Braude, head of infectious disease; Ted Danowski, one of the world’s premier diabetologists. And that was the rule; it wasn’t that I drew the lucky three. Today you would see no equivalent people—almost none—in a similar role.

PM: What is your personal process of discovery?

Kushner: The idea-development process that leads to the experiments, the manuscripts, and the grants comes from interaction with the people in your lab, your colleagues, your mentor. The inspiration for discovery comes from constant reading, constant observing, and constant interaction.

Hibbs: Science is a very communal activity, and we interact on many dimensions. We’re exposed to the ideas and the work of many different scientists, of many different nationalities. All of these go into the mix.

Brenner: For me, everything came at the end of the long day, in the quiet of the night, by replaying the tape that I went through in my waking hours. I have not spent a night since I was 25 years old without index cards on my night table. I go to work in the morning and just follow the leads of that digestion or reanalysis from the night before, thinking through how I should change [a study], do it differently. The data drive the steps day in and day out. Nothing else matters.

Braverman: Young people have one great advantage: Instead of index cards, there’s a database program. If I have 10,000 notes and 700 to 800 patients on a program, I can ruminant over the data, look at it from different perspectives. It makes it so much easier, so much more convenient.

PM: How would you advise people aspiring to careers like yours?

Brenner: The name of my game was to amass an enormous number of experimental models, to make measurements repeatedly, to the point where I could pretty much fashion the discipline. I didn’t have to look over my shoulder very much and didn’t have the stress of competition. After 25 years, I could rely to a large extent on younger colleagues I had trained. And that gave me time and the freedom to extend myself into other areas.

Kushner: Pick the right mentor. The key to beginning a career as an academic person is to get a career development award. It assures you protected research time. It takes a mentor to tell you how to write the grant, how to organize your thoughts.

Hibbs: I still approach basic biology like a child, with this almost naïve enthusiasm.

Brenner: If you’ve really excelled in your clinical training, then go into a basic laboratory and find that you know nothing—that the technicians are dominant, and you’re just learning how to mix solutions. When you go through that year depressed because nothing works, you’re breaking glassware, that’s when the mentor has to help you work on something where you can be successful.

PM: What are the prospects for the physician-scientist?

Brenner: The personal reward of a career in investigative medicine is second to none.

Braverman: My wife understood how important my work was to me, and we decided that despite the financial opportunities of private practice, we were going to stick with what I was doing in academic medicine. I’ve never regretted it.

Kushner: People who choose this path really have to have a terrific desire, a burning interest. And nothing will satisfy them other than testing their ideas and learning how to do the tests. I don’t know how our partners put up with us. I don’t go home very often.

Hibbs: If you’re really doing something that’s true investigation—and the more basic it is, the more risky it is in terms of really succeeding in uncovering new knowledge—there is this inherent risk that makes it very uncomfortable, but true adventure. Balancing this with clinical work can be tough.

Kushner: John, I remember a time when Françoise was urging you to spend more time at home. I came to your house, and you had moved part of your laboratory to the house.

You had a microscope set up next to the living room; you had plates; and you were working from home.

Brenner: That’s not what she had in mind.

Hibbs: I realized early on that I had to give up something, and what I gave up is academic travel. That way I could be a presence in my home as a husband and as a father.

Braverman: I used to take the kids to the lab and on rounds when they were young. They knew I wanted to be with them, and they had some notion as to what was going on. That was important.

PM: How do you feel about the prospect of retirement?

Brenner: I hate to confront it, which is why I tend not to. I spent 30 years doing mostly animal-oriented research. Then some very large clinical trials. Now I find myself in epidemiology, which I never would have guessed 20 years ago would have engaged me. I see my career just continuing to evolve. I pay less attention to the clock, with the hope that if my health stays good and my head stays reasonably good, this could continue for many years to come.

Hibbs: In a year or so, good lord willing, there will be time to do some other things—read philosophy and literature, spend time in France where my wife is from, walk in the Wasatch Mountains. We recently solved a major conceptual barrier in our research. Finishing this may open a new area for people to investigate, and I’ll be able to stop with a success.

Kushner: I’ve got some tasks to finish, to ensure the future of the people who depend on me and on whom I depend to be productive. It’s very hard to stop doing something you really like to do. We finally figured out the mechanism causing a type of porphyria. We have a lovely manuscript in PNAS [Proceedings of the National Academy of Sciences] now describing what goes on in the liver cell. And I’ve become a crystallographer in my old age.

Braverman: There are so many things I can do, that I want to do. But the one existential reality—I think we can all say—I strongly believe: We’ve had damn good lives. We’ve enjoyed our lives. They’ve been fulfilling, productive. That’s why I don’t really worry about the onset of age. I feel I can’t stop because I’ll end up depressed if I lose the things I love so much. It is a young man’s job. I’m getting up at 5 in the morning to hear night-phone admissions in Brooklyn, and it’s getting to be a little hard. But I just can’t stop.

Brenner: We’re the four horsemen—hopefully not of the apocalypse.
Patrick Fraizer’s heart was the size of a football. He didn’t know that, of course, or he wouldn’t have driven all the way from his home in Fort Wayne, Ind., to Pittsburgh. He wasn’t feeling as peppy as usual, but that’s why he was making the trip in the first place. Fraizer, a kind man with a ruddy face and enormous grin, had suffered two heart attacks in the past nine years. He was planning to meet with Pittsburgh cardiologists about an experimental cardiac therapy. He didn’t, however, know that things were as bad as they were.

When Fraizer arrived at the University of Pittsburgh Medical Center, doctors performed a routine catheterization to take a virtual snapshot of the condition of his heart. Then he and his wife, Mary Fraizer, waited around for the verdict. He was half-expecting to be sent back home. "We don’t think you can make it to the door," the doctors told him instead. They said it was a miracle that Fraizer was even alive—he had so much scar tissue on his heart from his previous heart attacks that
heart was barely functioning. Worse, two of his coronary arteries were fully blocked and another was disastrously close. The experimental therapy was a no-go. The doctors said instead they had to perform a much riskier open heart surgery—immediately.

That's when they discovered that his heart had swollen to the size of a football. Fraizer's previous heart attacks had, through the years, caused part of his heart muscle to balloon out. Often, the part of the heart that is starved of oxygen during an attack can become so damaged that it cannot do the work it used to do. The rest of the heart tries to make up for it, yet it can't always compensate. So the damaged part of the heart responds by thinning, ballooning, and stiffening. These reactions reduce the muscle's efficiency further and can lead to heart failure—something that Fraizer had been flirting with for years without even knowing it.

While Fraizer was having his heart resculpted in the operating room, William Wagner and colleagues were several blocks away exploring how to prevent the need for such operations in the first place. Wagner, the deputy director of the University of Pittsburgh—UPMC McGowan Institute for Regenerative Medicine, is a tissue engineer and Pitt professor of surgery, bioengineering, and chemical engineering. Along with Pitt colleague Michael Sacks, William Kepler Whiteford Professor of Bioengineering, Wagner oversees the development of a biodegradable heart patch that may one day prevent the long-term cardiac damage that Fraizer and others suffer after heart attacks. Wagner and Sacks' work was recognized by Scientific American as among the 50 most outstanding acts of leadership in science and technology in 2006.

Reportedly, heart tissue has been extremely difficult to engineer because of its mechanical properties. It is strong, yet flexible, and is more easily stretched in one direction than another, depending on the direction in which its fibers are aligned. In addition, the body is sensitive to the introduction of foreign materials that don't quite match heart tissue's natural properties.

In his office, Wagner is surrounded by old journal issues, images of blood vessels, a whiteboard on which someone has scribbled circuit diagrams and graphs, three cacti (remnants of a youth spent in Phoenix), and numerous photos of his two young boys. Someone wandering in might wonder whether he is a scientist or an engineer, a surgeon or a chemist. Wagner thinks of himself as a translator between the worlds of engineering and medicine. Through the years that has meant working closely with patients, doctors, and other types of scientists.

"The way I describe it is as engineering applied to address cardiovascular disease," Wagner says of his work.

Engineering cardiac tissue in the lab requires expertise in many areas—mechanical and materials engineering, chemistry, molecular biology, immunology, and surgery, to name a few. Pitt stands out, observers say, because it has established a cadre of experts who work cohesively together.

"That's really how high-impact science is being done nowadays," Wagner says. "It's being able to assemble teams of experts where you have world leaders in different areas coming together and hashing out ideas."

"They have really made things happen," says Kim Woodhouse about Pitt's cardiac bioengineers. Woodhouse is a professor of engineering and applied chemistry at the University of Toronto. The Pitt team is pragmatic, synergistic, and creative, she says, and this combination puts them right "at the leading edge."

Wagner first became interested in applying engineering to medicine when he was in graduate school for chemical engineering at the University of Texas at Austin. One day, when listening to an engineering professor talk about his work on blood clots, Wagner suddenly saw how the engineering science that he'd learned as an undergraduate could be applied to the human body.

"I immediately knew that's what I wanted to do," he says.

He graduated with a PhD in chemical engineering, after having spent many a Saturday at the Texas Medical Association Library, slouched over medical journal articles. Then Wagner got an unexpected call from a surgeon at the University of Pittsburgh looking to hire a postdoctoral fellow to study blood clots and artificial hearts.

"And I'm thinking, Pittsburgh? I'm from Arizona," says Wagner with a laugh. Nevertheless, he visited.

"Within a couple of meetings with people, I realized that it was kind of like Mecca," he recalls. The problems he had only seen on microscope stages or in library cubicles in Texas were right in front of him at Pitt, having a "very real impact on patients every day," he says. He accepted the position.

At that point, Wagner wasn't quite ready to step up to the role of translator—he was, literally, still learning the language of medicine. "I knew a lot of the terms, and I'd read them dozens of times," he says, "but I'd never actually heard them pronounced!" As he immersed himself, he started noticing an interesting trend: Some medical terms were oddly vague, and the reason for this, he realized, was that no one really understood the processes they were trying to describe. That, he thought, was a hole that engineering could help fill.

Wagner, along with Michael Sacks, a PhD biomechanical engineer with a dry sense of humor and an astute eye for detail, began closely studying the mechanics of cardiac processes, an area Sacks first started researching in graduate school at the University of Texas Southwestern Medical Center at Dallas. The heart can be thought of as a machine, and Wagner and Sacks wanted to understand it inside and out so that they could, in a sense, reverse-engineer parts of it. Wagner and Sacks realized there was a huge medical need for engineered cardiac tissue. Other bioengineers have typically used materials that poorly mimic the properties of cardiac tissue—so Wagner decided it was up to his team to develop something better.

The engineers imagined developing a cardiac patch that could help damaged hearts repair themselves. This patch would work best, they theorized, if it could mimic the type of temporary scaffolds the body makes on its own all the time.

"When you cut yourself, you make a clot, and then you put a temporary scaffold in there," Wagner explains. Then special immune cells arrive, release enzymes that help the tissue regenerate, and clear the temporary scaffold away.

But when the heart gets injured during a heart attack or because of other defects, it might not be able to repair itself. Instead, it might respond the way Fraizer's heart did—by ballooning out, which causes further problems and makes the heart even less efficient. Wagner and his team then wondered whether it would be possible to create a synthetic scaffold that, if applied to the heart within a few weeks of a heart attack, could allow the heart to repair itself.

They went to work. One of Wagner's postdoctoral fellows, Jianjun Guan, created a polyurethane material that was nontoxic, highly elastic, strong, and biodegradable. Polyurethane is the stuff of seat cushions, and Wagner explains that, like a good cushion, the material is strong yet flexible, able to bounce back after being compressed or stretched. His team found ways to manipulate the material so that it stretches more in one direction than the
While developing their überpatch, Wagner's team made a serendipitous discovery. They were testing the effects of a patch on rats that had experienced recent heart attacks when the team found that even without stem cells, the patch improved heart performance.

“That’s a lot more attractive and a lot closer to clinic than messing around with stem cells,” Wagner says. A plain patch would not have to undergo as much testing for approval by the FDA, he says, and it could be implanted without first having to harvest cells from the patient.

That the patch worked well by itself was unexpected, but Wagner has some ideas as to why. First, the patch acts like a kind of girdle, he notes, preventing the injured heart from ballooning out as it tries to heal. This keeps heart cells healthier, so they are less likely to die. Second, as the body’s immune cells come into contact with the patch, they might release enzymes that help the heart heal faster.

In the past, engineers have designed heart patches out of permanent materials like Gore-tex. If doctors use Gore-tex patches to treat children born with heart defects, “the kid’s going to grow and [the patch is] not going to grow, so they’re going to have to go in and keep changing it out in many instances,” Wagner says.

In older patients, Gore-tex patches applied to help support the weakened heart wall after a heart attack present other problems. In these cases, surgeons must open the heart and place the Gore-tex patch on the inside surface. Wagner’s patch does not require such risky surgery; it is fastened to the outside surface of the heart, a less invasive procedure.

Blood contact with foreign materials can trigger clot formation and these clots can break free and cause strokes. So patients with Gore-tex patches often have to take blood thinners. But the Pitt patch avoids blood contact and, by design, clotting and the need for blood thinners.

The Pitt team has also figured out a way to manufacture tissue scaffolds quickly, both with and without seeded cells. This breakthrough is important clinically and could have implications beyond a cardiac patch. The method could be useful for engineering other thin, just like real cardiac tissue—and so that it can degrade at different rates after coming into contact with particular bodily enzymes. The team found ways to make the material release growth factors to promote cell growth and differentiation. All the better, the material is easy to make.

“An undergraduate chemistry major could be taught to do it,” Wagner says.

At the same time, Sacks studied the mechanical properties of heart tissue. How would a synthetic patch need to behave in order to closely mimic real cardiac tissue?, he wanted to know. Wagner collaborated with investigators working with stem cells—including Pitt’s Johnny Huard, who is a PhD and the Henry J. Mankin Professor of Orthopaedic Surgery Research, and assistant professor of surgery Amit Patel, an MD—to eventually “seed” or embed the synthetic scaffold with patient cells that could later be coaxed into developing into functional heart cells. Wagner and Sacks imagined a seeded patch that could be sutured onto a person’s heart—not a particularly invasive procedure, because the heart does not need to be cut—and restore working function to the muscle.

While developing their überpatch, Wagner’s team made a serendipitous discovery. They were testing the effects of a patch on rats that had experienced recent heart attacks when the team found that even without stem cells, the patch improved heart performance.

“That’s a lot more attractive and a lot closer to clinic than messing around with stem cells,” Wagner says. A plain patch would not have to undergo as much testing for approval by the FDA, he says, and it could be implanted without first having to harvest cells from the patient.

That the patch worked well by itself was unexpected, but Wagner has some ideas as to why. First, the patch acts like a kind of girdle, he notes, preventing the injured heart from ballooning out as it tries to heal. This keeps heart cells healthier, so they are less likely to die. Second, as the body’s immune cells come into contact with the patch, they might release enzymes that help the heart heal faster.

In the past, engineers have designed heart patches out of permanent materials like Gore-tex. If doctors use Gore-tex patches to treat children born with heart defects, “the kid’s going to grow and [the patch is] not going to grow, so they’re going to have to go in and keep changing it out in many instances,” Wagner says.

In older patients, Gore-tex patches applied to help support the weakened heart wall after a heart attack present other problems. In these cases, surgeons must open the heart and place the Gore-tex patch on the inside surface. Wagner’s patch does not require such risky surgery; it is fastened to the outside surface of the heart, a less invasive procedure.

Blood contact with foreign materials can trigger clot formation and these clots can break free and cause strokes. So patients with Gore-tex patches often have to take blood thinners. But the Pitt patch avoids blood contact and, by design, clotting and the need for blood thinners.

The Pitt team has also figured out a way to manufacture tissue scaffolds quickly, both with and without seeded cells. This breakthrough is important clinically and could have implications beyond a cardiac patch. The method could be useful for engineering other thin,
elastic tissue in the body, such as bladders, as well as tube-like structures like the urethra and esophagus.

Although Fraizer’s surgery went well—and his hospital recovery was sweetened upon learning that he would soon be a grandfather for the first time—his heart will forever be weak. “If I see 65, I’ll be a blessed man,” he says, now almost 61.

Perhaps 10 years from now, if all goes well in the laboratories at McGowan, a patient with Fraizer’s heart condition will be able to live a lot longer than that. Wagner and Sacks will be testing the patch, with and without live a lot longer than that. Wagner and Sacks will be testing the patch, with and without stem cells, in large animals and humans over the next few years.

After his second triple-coronary-bypass surgery in 2002, then-43-year-old Douglas Laney was told by his doctors that there was nothing more they could do. Even two triple bypasses hadn’t fixed his problem permanently. The average lifespan of a vein graft is seven to 10 years—a lifespan that diminishes with every additional bypass surgery. So Laney was scared, especially when he began having chest pain again last year.

“I didn’t know what to do,” he says. But he did do something: He got a second opinion.

After performing a catheterization, the doctors treating Laney visited him in his recovery room. Laney was waiting anxiously, afraid of what they might tell him. But the doctors delivered good news: They were willing to take the chance that his previous doctors refused to take. They were willing, they said, to try to perform another bypass.

“I experienced probably every human emotion within five minutes,” Laney says. “I was overwhelmed with joy.”

In patients with clogged arteries, bypasses usually fail because the replacement veins, which are often nonessential veins taken from another part of the body, aren’t up to the job.

Veins are used to living “a pretty cushy lifestyle,” according to Pitt vascular engineer David Vorp, and are not prepared for the demanding arterial environment. Veins are used to low blood pressure and low flow, and they don’t feel the pulsations of the heart. Arteries, on the other hand, have higher blood flow, higher shear stresses, and they pulsate because of their proximity to the heart. So when veins from the leg are plugged into the arterial environment, they tend to panic.

“They say, ‘Wait a minute, we’re veins, we’re not supposed to be experiencing this,”’ says Vorp, an associate professor of surgery. He explains that a vein implanted into the arterial environment assumes that it is injured, so it immediately begins trying to counteract the problem. It does so by thickening. As it thickens, however, the canal also begins to narrow. Sound familiar?

“You end up having the exact same problem as you had before. You have narrowing and clotting off of the blood flow, and that’s one of the primary failure mechanisms of vein grafts.” Vorp says.

That’s exactly what happened to Laney after his first two bypasses—his grafts failed. Although he was understandably nervous about going in for another triple bypass, he says that, psychologically, it was easier the third time around. “This time, I had reached a point of acceptance that what was going to happen was going to happen,” he says. Luckily, the surgery was a success; even so, he can’t be as active as he once was, though he likes to help out with his church and do other volunteering. And there is always the fear that the grafts could fail again.

Vorp, who is soft-spoken and sports a red-golden beard, hopes that his collaboration with Wagner will eliminate the need for repeat bypass surgeries by making implanted veins stronger. If the vein to be used in bypass surgery is first wrapped in a biodegradable polymer material like the one developed for Wagner and Sacks’ cardiac patch, it may not thicken as much upon exposure to its new environment. Then, after a few days perhaps, the wrap degrades, allowing the vein to slowly adapt to its new harsh environment. The vein girdle has a patent pending.

Vorp describes himself as being “born, bred, raised, trained, and differentiated, if you will, in Pittsburgh.” What actually “differentiated him from a typical mechanical engineer into a bioengineer was a class he was required to take as a Pitt student. “This silly little course, that I tried to put off and tried to get out of taking, pretty much changed my life,” he says. In it, he was required to write a report on how mechanical engineering impacts society. When he explained this to his girlfriend at the time, who was in dental school, she noted that mechanical engineering plays a big part in dentistry. That piqued his interest.

“I went to the library, and I stumbled across two journals. One was the Journal of Biomechanics, and the other was the Journal of Biomechanical Engineering. I just was devouring these, and I thought it was the coolest thing,” he recalls.

At the time, Pitt didn’t have a bioengineering department, but Vorp was able to get a research position after graduation working with bioengineer Harvey Borovetz, who was then in the Department of Surgery. That’s where Vorp developed his expertise in vascular bioengineering. He also worked closely with patients and doctors in the artificial heart program.

The “bread and butter” of Vorp’s work these days is studying the mechanics of the abdominal aortic aneurysm, a condition in which the large blood vessel supplying blood to the lower body becomes abnormally large. Vorp is developing noninvasive ways to predict which types of aneurysms are at risk of bursting.

He also is trying to develop fully synthetic arteries using tiny biodegradable polymer-based tubes that can be seeded with stem cells. He wants to coax the stem cells to develop into vascular cells. Then, as the polymer breaks down after implantation, the cells would take over and create a complete blood vessel. If his team can find a way to do this, it will have become the first to create a successful artificial artery.

Asked how long it will be before all of these procedures, including the vein girdle, are tested in humans, Vorp laughs, saying, “It’s funny, it seems like every time someone asks me how far away we are from clinical translation, I say five years. I said that 10 years ago, and I said that five years ago.” Then he smiles. “This is probably the first time that I can think about it and believe that it’s going to be less than five years.”

Wagner and Sacks are also pursuing other projects. For example, they are developing an engineered heart valve using the same polyurethane material as the patch. Although it will be a year or two before they begin testing it in small animals, the mechanical properties of their engineered valve seem to match natural valves.

The value of life has become even clearer for Fraizer since his surgery. Although his heart is no longer as big as a football, metaphorically, it still seems to be. He pours as much of it as he can into his 1-year-old granddaughter, BreAnna, whom he babysits every day. He admits that he spoils her a little, but, he says, that way she will always know she only deserves the best.

“Things really do blossom out of tragedy,” he says. “I absolutely love being around this girl.”

“What we are doing,” says Vorp, reflecting on his work one day recently, “is really trying to make life happen.”
MATCH RESULTS CLASS OF 2007

ANESTHESIOLOGY
Espin, Stephen
UPMC Medical Education Program

Gabriel, Jessica
Western Pennsylvania Hospital

Gralis, Benjamin
UPMC Medical Education Program

Knech, Garrick
UPMC Medical Education Program

Lin, Charles
UPMC Medical Education Program

McCreary, Justin
UPMC Medical Education Program

Victor-Vega, Cassandra
University of Rochester/ Strong Memorial Hospital, N.Y.

Wedsich, Audra
UPMC Medical Education Program

Zehnbub, Alon
Harbor-UCLA Medical Center, Calif.

DERMATOLOGY
Carlos, Casey
Hospital of the University of Pennsylvania

Koen, Sonnery
University of Maryland Medical Center

Patali, Shalay
University of Chicago Medical Center, Ill.

DIAGNOSTIC RADIOLOGY
Gage, Kenneth
Johns Hopkins Hospital, Md.

Ho, Andrew
University of Chicago Medical Center, Ill.

Kantaritz, Stamatis
UPMC Medical Education Program

Patali, Amish
Henry Ford Health Science Center, Mich.

Sy, Su-hun
Albany Medical Hospital, Pa.

Whitson, Joseph
Oregon Health & Science University

EMERGENCY MEDICINE
Abdennour, Enzo
Barnes-Jewish Hospital, Mo.

Barnes, Joseph
UC Davis Medical Center, Calif.

Brown, Emily
Brigham & Women's Hospital, Mass.

Cochran, Kristin
Beth Israel Deaconess Medical Center, Mass.

Connors, Megan
Stanford University Programs, Calif.

Ferreri, Gregory
Christiana Care Health Services, Del.

Pousson, Amelia
Christiana Care Health Services, Del.

Rivens, Matthew
UPMC Medical Education Program

Roberts, Lindsey
Beth Israel Deaconess Medical Center, Mass.

Shetty, Pranev
Harbor-UCLA Medical Center, Calif.

Shokr, Aaron
Brigham & Women's Hospital, Mass.

Solakovski, Devin
Rhode Island Hospital/Brown University

Tart, Carly
Albany Medical Hospital, Pa.

Terraz, Jennifer
Christiana Care Health Services, Del.

Whelser, Matthew
UPMC Medical Education Program

FAMILY PRACTICE
Barragan, Lorenzo
MacNeal Memorial Hospital, Ill.

Butler, Heather
Oregon Health & Science University

Farahi, Narges
University of California, San Francisco

Izmir, Erin
UPMC St. Margaret

LeBlanc, Karen
Memorial Hospital of Rhode Island/Brown University

Lewis, Allison
Barnes-Jewish Hospital, Mo.

McDowell, Mark
Beth Israel Medical Center, N.Y.

MEDICINE—PEDIATRICS
Mittal, Chad
UPMC Medical Education Program

IMMUNITY—PEDIATRICS
McConkey, Andrew
UPMC Medical Education Program

INTERNAL MEDICINE—PRELIMINARY
Weiss, Michael
UPMC Medical Education Program

INTERNAL MEDICINE—PRIMARY
Oklahoma, Craig
Brigham & Women's Hospital, Mass.

INTERNAL MEDICINE—WOMEN'S HEALTH
Osterhout, Christine
UPMC Medical Education Program

Tatara, Sarah
UPMC Medical Education Program

MAXILLOFACIAL SURGERY
Nehs, Craig
UPMC Medical Education Program

NEUROLOGICAL SURGERY
Benzhoff, Christopher
UPMC Medical Education Program

NEUROLOGY
Miller, Brian
UPMC St. Margaret

Phelps, Tracey
UPMC St. Margaret

Sullivan, Brian
Scarpa Mercy Hospital Chula Vista, Calif.

Wilk, Matthew
Washington Hospital, Pa.

INTERNAL MEDICINE
Agarwal, Cecily Marie
University of Maryland Medical Center

Brahmashund, Vikram
Boston University Medical Center, Mass.

Cheung, Sonia
University of California, Davis

DuVito, Nicholas
Thomas Jefferson University, Pa.

Falk, Eric
Yale-New Haven Hospital, Conn.

Gascon-Flors, Alegria
Harbor-UCLA Medical Center, Calif.

Kagan, Seth
Santa Clara Valley Medical Center, Calif.

Koprowski, Michael
UPMC Medical Education Program

Muth, Katarzyna
Oregon Health & Science University

Mazzarella, Dara
University of Michigan Hospitals—Ann Arbor

Mollica, Mary
New York University School of Medicine

Nayak-Huchemi, Harini
UPMC Medical Center, Calif.

Pan, Stephen
Stanford University Programs, Calif.

Rachakonda, Vikrant
Barnes-Jewish Hospital, Mo.

Rao, Shovder
University of Michigan Hospitals—Ann Arbor

Ravilla, Shilpa
Boston University Medical Center, Mass.

Sabatini, Michael
UPMC Medical Education Program

Sawatsoy, Adam
Mayo School of Graduate Medical Education, Minn.

Singh, Deeya
University of Chicago Medical Center, Ill.

Staub, Brian
UPMC Medical Education Program

Stephenson, Lydia
UPMC Medical Education Program

Swan, Christopher
University of California, San Francisco

Tan, Roderick
UPMC Medical Education Program

Tu, Benjamin
Johns Hopkins Bayview Medical Center, Md.

Williams, Vincent
SUNY Health Science Center—Brooklyn, N.Y.

INTERNAL MEDICINE—PEDIATRICS
McConkey, Andrew
UPMC Medical Education Program

MERCHANT—PEDIATRICS
Olive, Ashley
UPMC Medical Education Program

NURSE—PEDIATRICS
Ehrlich, Lori
UPMC Medical Education Program

Berger, Loretta
Children's Hospital of Philadelphia, Pa.

PEDIATRICS
Gilbert, Christopher
UPMC Medical Education Program

Huang, Epidict
UPMC Medical Education Program

Luo, Alvin
University of California San Diego Medical Center

Shridhar, Matthew
UCLA Medical Center, Calif.

OBSTETRICS/GYNECOLOGY
Brannen, Ryan
Drew University College of Medicine, Pa.

Chong, Melissa
White Memorial Medical Center, Calif.

Gonzalez, Kelly
UPMC Medical Education Program

Jones, Candice
Walter Reed Army Medical Center, D.C.

Krajewski, Colin
Case Western Reserve Medical Center, Ohio

Landis Lewis, Deborah
UPMC Medical Education Program

O'Neill, Erica
University of North Carolina Hospitals, Chapel Hill

Phillibert, Donald
Stony Brook Teaching Hospitals, N.Y.

Sakamoto, Sara
UPMC Medical Education Program

OPTOMETRY
Ho, Andrew
UPMC Medical Education Program

Naidu, Shrinivas
Pennsylvania State University–Hershey

Singh, Deeya
University of California, San Francisco

ORTHOPAEDIC SURGERY
Frank, Matthew
UMORS—New Jersey Medical School

Heffernan, Michael
University of Massachusetts Medical School

Starnes, James
Carolinas Medical Center, N.C.

Vanderkooi, Corinne
New York–Presbyterian Hospital—Columbia

Williams, Vincent
UPMC Medical Education Program

OTOLARYNGOLOGY
Dhansaji, Shilpa
UPMC Medical Education Program

Jabbour, Noel
University of Minnesota Medical School

Kim, Hana
Northwestern McGraw/NMV/VA, Ill.

Kraechlin, Cheryl
UPMC Medical Education Program

Rodriguez, Kenneth
UPMC Medical Education Program

PEDIATRIC SURGERY
Gibert, Christopher
UPMC Medical Education Program

Miller, Jennifer
UPMC Medical Education Program

PHYSICAL THERAPY
Berger, Loretta
Children's Hospital of Philadelphia, Pa.

Henderson, Louis
UPMC Medical Education Program

Scarpa Mercy Hospital Chula Vista, Calif.

VET NAME
Vet Practice
University of Kentucky

Surgical Program
UPMC Presbyterian Shadyside

PATHOLOGY
Gascon-Flors, Alegria
Harbor-UCLA Medical Center, Calif.

Ogagaon, Pepple
UPMC Medical Education Program

Barragan, Lorena
Scarpa Mercy Hospital Chula Vista, Calif.

WHELSTON, Joseph
Oregon Health & Science University

EMERGENCY MEDICINE
ASHLEY, David
Brigham & Women's Hospital, Mass.

GOLGORSKY, Yakov
Barnes-Jewish Hospital, Mo.

HAYES, Logan
UPMC Medical Education Program

JABBOR, Noel
University of Minnesota Medical School

JABOUB, Joanna
University of California, San Francisco

KRAECHLIN, Cheryl
UPMC Medical Education Program

LEWIS, Deborah
UPMC Medical Education Program

O'NEILL, Erica
University of North Carolina Hospitals, Chapel Hill

Sakamoto, Sara
UPMC Medical Education Program

SCHERBERK, Jennifer
UPMC Medical Education Program

Surgical Program
UPMC Presbyterian Shadyside

MEDICINE
IMMER, Erin
UPMC St. Margaret

New York University School of Medicine

SCHOLNIK, Aaron
Brigham & Women's Hospital, Mass.

SINGH, Deeya
University of California, San Francisco

SCHOLNIK, Aaron
Brigham & Women's Hospital, Mass.

SONG, Min, Stuart
UPMC Medical Education Program

SOLOKOWSKI, Devin
Rhode Island Hospital/Brown University

SINGH, Deeya
University of California, San Francisco

SOLAKOWSKI, Devin
Rhode Island Hospital/Brown University

SONG, Min, Stuart
UPMC Medical Education Program

SOUTHEY, Pranev
Harbor-UCLA Medical Center, Calif.

SPRAIN, Cameron
University of California, San Francisco

SUMMER 2007

33

imp-687-F 17/01/07
Her name is Majta Seiden. In the photograph, she’s 18 years old. The Seidens were among 106 Jewish families studied in the spring of 1942 in Tarnow, Poland, by a team of Austrian anthropologists researching the “race biology” of Polish Jews. Its purpose, the study’s lead author wrote, was to form the “basis for relocation and new settlements” of Jews in the Reich. In the course of 10 days, the anthropologists measured noses, skulls, and torsos. They recorded the color of eyes, skin, and hair. They took fingerprints, handprints, and detailed family medical histories. They drew blood.

The researchers took photos of Majta, her parents, and her two younger brothers. Each of the subjects posed for photos from three angles—in profile, at 45 degrees, and facing the camera directly. When Majta faces the camera, her lips are upturned at the corners, ever so slightly.

A few months after this photo was taken, by June of 1942, more than half the Jewish population of Tarnow had been sent to the concentration camp in nearby Belzec. Historians believe the Seidens would have all died in the camp.

Viewed on a museum wall decades later, the Seiden photos are a stark example of the human toll of Nazi Germany’s eugenics movement. The Nazi obsession with genetics rationalized mass sterilization and euthanasia of the mentally ill and otherwise disabled and gave “intellectual” and material support to the Holocaust. “Deadly Medicine: Creating the Master Race”—a documentary exhibition at The Andy Warhol Museum this winter sponsored by UPMC and organized by
the United States Holocaust Memorial Museum in Washington, D.C.—shows science’s role in the campaign.

The exhibition is slated for a multiyear national tour. In its Pittsburgh launch, “Deadly Medicine” included several programs held in collaboration with the University of Pittsburgh that delved into the legacy of eugenics that has left to modern medicine. Pitt’s Margaret McDonald, associate vice chancellor for health sciences academic affairs, Lisa Parker, associate professor of human genetics, and David Barnard, professor of medicine, worked with the Warhol to offer a series of public talks and forums at the museum. (These were on the heels of a Scaife Hall lecture by Susan Bachrach, curator of the exhibition; her December visit was sponsored by the C.F. Reynolds Medical History Society.) The Warhol talks featured Pitt medical geneticists, public health experts, physicians, bioethicists, art historians, and even a poet. On February 20, Arthur S. Levine, senior vice chancellor for the health sciences and dean of the medical school, hosted a Dean’s Summit that drew academic medicine representatives from Pennsylvania, Maryland, Georgia, West Virginia, Ohio, and Washington, D.C. The School of Medicine also offered its students a “Deadly Medicine” minielective with a discussion and private exhibition tour led by Bachrach and Pitt’s Marta Kolthoff, assistant professor of obstetrics, gynecology, and reproductive sciences.

The programs were cautionary in nature, reflecting the tone of the exhibition. “Deadly Medicine” shows how well-respected scientists helped prosecute mass murder, says Bachrach. “The prevailing image of Nazi medicine is that they were fanatics and political zealots, that they weren’t mainstream.” That’s not the case, she says.

The exhibition documents the growth of eugenics from its roots in 19th-century social Darwinism. In the United States, eugenics gained popularity at a time when its proponents claimed that the “feebleminded” and immigrants from Southern and Eastern Europe weakened the country’s genetic stock. Writing books with Brave New World–like titles, such as Sterilization for Human Betterment, geneticists in the United States argued to cull the gene pool of those with “less desirable” traits. They even prevailed upon the country’s highest court.

“Three generations of imbeciles are enough,” wrote Supreme Court Justice Oliver Wendell Holmes in Buck v. Bell, the 1927 decision allowing Virginia officials to sterilize Carrie Buck, an unwed mother with an alleged family history of mental retardation. From 1909 to 1933, 16,000 people in this country were sterilized, many of them wards of state psychiatric institutions. The practice continued into the 1970s; by then, 65,000 people had been sterilized.

In the wake of a diminishing birthrate after World War I, Germany stressed fertility. The public health message merged with the racist and nationalist belief that the Nordic “race” was ideal. As the Nazis consolidated their power, a eugenics movement also took hold. “Deadly Medicine” shows the inexorable slide of German eugenics toward mass murder. The viewer sees still photos of sterilization operations before an amphitheater of German medical students. From 1933 to 1945, state doctors sterilized 400,000 disabled and mentally ill Germans, deemed “life undeserving of life.”

The 1933 Erbgesundheitsgesetz, or law concerning hereditary health, paved the way for such sterilizations, points out Pitt’s Loren Roth, senior associate vice chancellor, health sciences and professor of psychiatry and of health services administration. Roth, who participated in the Dean’s Summit, notes that the field of psychiatry was complicit in this campaign. (He also notes that psychiatrists who objected to the practice were removed from their positions.)

Elimination of those deemed “incurable” would come next. Physicians and midwives referred children born with mental or physical defects to special pediatric euthanasia units, which killed 5,000 children. The exhibition includes a stark, metal, white crib, like those used in the units. It sits empty.

Not content with preventing “undesirable offspring,” the Reich soon targeted the adult disabled population for extermination. From 1939 to 1945, the state killed some 200,000 Germans—the most incapacitated of those housed in state asylums. To accomplish this, Nazi doctors developed efficient killing strategies, placing victims in gas chambers and burning their corpses in crematoria. That set the stage for the “Final Solution” and the annihilation of 6 million. Doctors were there every step of the way; the exhibition reminds us.

“Deadly Medicine” raises enduring questions: How could medicine become such a hand servant of evil? What would each of us do if confronted with a similar situation?

The programs urged participants to consider whether our society is pursuing questionable ideals of biological perfection in its own way, through plastic surgery, the testing of fetuses, or whatever advances medical science has in store.

Pitt School of Law Dean Mary Crossley, whose own scholarship focuses on healthcare inequalities, offered words of caution in her Warhol talk. She worries about an implicit bias against sickness and imperfection.

“We really need to be very attentive to the choices we’re making,” says Crossley, “and [make sure] they promote not only the welfare of society, but also individual welfare and freedom.”

Elimination of those deemed “incurable” would come next. Physicians and midwives referred children born with mental or physical defects to special pediatric euthanasia units, which killed 5,000 children. The exhibition includes a stark, metal, white crib, like those used in the units. It sits empty.

Not content with preventing “undesirable offspring,” the Reich soon targeted the adult disabled population for extermination. From 1939 to 1945, the state killed some 200,000 Germans—the most incapacitated of those housed in state asylums. To accomplish this, Nazi doctors developed efficient killing strategies, placing victims in gas chambers and burning their corpses in crematoria. That set the stage for the “Final Solution” and the annihilation of 6 million. Doctors were there every step of the way; the exhibition reminds us.

“Deadly Medicine” raises enduring questions: How could medicine become such a hand servant of evil? What would each of us do if confronted with a similar situation?

The programs urged participants to consider whether our society is pursuing questionable ideals of biological perfection in its own way, through plastic surgery, the testing of fetuses, or whatever advances medical science has in store.

Pitt School of Law Dean Mary Crossley, whose own scholarship focuses on healthcare inequalities, offered words of caution in her Warhol talk. She worries about an implicit bias against sickness and imperfection.

“We really need to be very attentive to the choices we’re making,” says Crossley, “and [make sure] they promote not only the welfare of society, but also individual welfare and freedom.”

Yet, Barnard reminded, some scientists still pursued highly dubious studies in the States. In 1974, the federal government mandated that universities establish institutional review boards to oversee human subject research.

It’s hard to imagine the Seidens anticipated what awaited them in 1942 as they sat for their portraits. The scientists studying them probably had some idea.

“We don’t know what measures about the expulsion of the Jewish People are planned in the next months,” wrote one researcher to another, “which, under certain circumstances, if we wait too long could deprive us of valuable material.”
CLASS NOTES

’50s When Roland Nord started practicing medicine in New Castle, Pa., he would get a call in the middle of the night if one of his patients ended up in the emergency room. It was his job, as a family physician, to go to the ER and care for his patients. That changed long ago with the advent of the ER physician. But Nord (MD ’55) is still practicing in New Castle, more than 50 years after graduating from medical school. A grateful patient of 38 years noted the milestone in 2005 and alerted the local newspaper, which promptly sent a reporter to Nord’s office. In a care of his patients in the Greenfield neighborhood of Pittsburgh, which is his home. Although he enjoys the warm response his work receives, it is occasionally too familiar. Patients and neighbors might show up on his doorstep for last-minute physicals or cold remedies.

While reading a magazine in 1999, critical care specialist Martin Doerfler (MD ’82) learned of a few Johns Hopkins professors who were ICU innovators. The following year he joined their fledgling company, VISICU, and is now a vice president for clinical operations there. The company’s eICU solution program combines information technology and staff training to reduce mortality and mistakes in the ICU.

Since completing his residency at UPMC Shadyside, Bernard Bernacki (Family Practice Resident ’84) has treated patients in the Greenfield neighborhood of Pittsburgh, which is his home. Although he enjoys the warm response his work receives, it is occasionally too familiar. Patients and neighbors might show up on his doorstep for last-minute physicals or cold remedies.

’90s When the radio crackled and the operator said that there was a car over the mountainside, David Sherwood (MD ’90), a family practice physician in rural Colorado, knew that the driver probably needed treatment as soon as possible. Sherwood arrived first at the scene of the accident. He saw an overturned car about 500 feet down the mountainside, so he grabbed his jump kit and roped down. After reaching the car and finding it unoccupied, he began to search the nearby brush, eventually finding a woman, splayed on a rock, unresponsive. She had been lying there 12 hours. Sherwood stabilized her before the mountain rescue team arrived with a helicopter to transport her to the nearest trauma center, about 110 miles away. (She later recovered.) Sherwood is one of three doctors for a clinic—which he owns—that treats about 3,000 people in the San Juan Mountains of Colorado. Serious car accidents like this occur about every other month, says Sherwood, medical director of Ouray County Search and Rescue. His clinic is about 30 miles from the nearest hospital. If a patient can’t pay, Sherwood has been known to

MARTIN SPRINGER
PUMP UP THE GAMOW BAG

Martin Springer (MD ’82) wants all his classmates to know: If you are ever in China, you really ought to look him up. Rather than settling down and starting a family, Springer long ago opted for packing his bags and starting a family.

At the University of Chicago, he completed the emergency medicine residency he began at Pitt. He later worked at the Chicago Medical School’s teaching hospital on the boundary of competing gangs. “We saw a lot of trauma,” he writes of the six years he was in Chicago, “some of it inflicted in the ER waiting room.”

During those years, Springer took two four-month breaks to work in Nepal, caring for locals and tourists. At the clinic near Mount Everest, he and his colleagues introduced the Gamow Bag, a portable, hyperbaric chamber used to treat altitude sickness. Filled with air by a pump used to inflate a raft, it looks like an inflated duffel bag big enough to hold a person, and it’s now standard issue on high-altitude expeditions.

A few years later, Springer relocated to Kathmandu with his wife and son and joined the staff of the CIWEC Clinic Travel Medicine Center, which cares for tourists, expatriates, and members of the diplomatic community. There he saw infectious diseases from
accept elk steaks or other services as payment.

Anita Courcoulas (General Surgery Intern ‘89, Surgery Resident ‘95, Pediatric Surgery Fellow ’96, Minimally Invasive Surgery Fellow ‘00) leads Pitt’s Division of Minimally Invasive Bariatric and General Surgery. Courcoulas studies the outcomes of bariatric surgery through several National Institutes of Health grants. Because of several common side effects—including nausea, dehydration, mood change, hair loss, and excess skin—she says it’s important that researchers continue to delve into these areas. She serves as principal investigator on a longitudinal study of bariatric surgery in children. The methodology paper on the study came out in April.

During his residency at Magee-Womens Hospital of UPMC, Richard Legro was inspired by David Guzick, Magee’s director of the Division of Reproductive Endocrinology at the time, who shared his love of medical research. When Legro (Obstetrics and Gynecology Resident ‘92) published a paper in The New England Journal of Medicine this year examining the common treatments for polycystic ovary syndrome (PCOS), he was pleased to see that Guzick—now dean of the University of Rochester School of Medicine and Dentistry—wrote the accompanying editorial. Legro is a professor of obstetrics and gynecology at Pennsylvania State University in Hershey, Pa.

Levi Downs (MD ’94), assistant professor of obstetrics, gynecology, and women’s health at the University of Minnesota, is glad there is now a vaccine to prevent women from contracting human papillomavirus (HPV), which causes most cervical cancers. But he notes the vaccine won’t help women who already have the virus and are susceptible to cervical cancer. He is investigating ways to shut down the proteins in HPV that cause the growth of new blood vessels that feed tumors. He experiments with RNA interference to stop the mechanism.

Doug Schuerer (MD ’95), an assistant professor of surgery at Washington University in St. Louis, researches a number of common problems that trauma surgeons see there, such as ATV and hunting accidents and blood infections. He has been named medical director of trauma at Barnes-Jewish Hospital and says he enjoys trauma surgery because it allows him to operate on the whole body. In January, he advocated for a Missouri bill proposing fines for drivers who don’t wear seat belts. He and his wife, Nickie Kolovos (MD ’96)—spotlighted in our Fall 2006 “The Way We Are”—expect their first child in July.

—Meghan Holohan & Chuck Staresinic

A Brahman offers blessings to Springer (in blue) before the doctor kayaks down the Kali River along the western border of Nepal.

Sherwood grabs his jump kit and disappears down the mountain.

all over the world, including typhoid, trypanosomiasis, schistosomiasis, malaria, dengue fever, visceral leishmaniasis, and Japanese encephalitis, to name a slew.

Playtime was also an adventure.

“I was lucky enough to be able to visit many of the remote parts of Nepal, kayak its rivers, and spend time with well-known members of the climbing and adventuring community,” he writes.

Today, Springer is chair of the emergency department in a rapidly growing private-venture hospital in Beijing. His outdoor pursuits now take him to remote Mongolia, where, “Instead of Nepali tea and coconut biscuit, it is alcoholic fermented mare’s milk and dried, rock-hard cheese.”

Where will Springer be in a few years’ time? Good question. He is looking forward to the 2008 Summer Olympics in Beijing. But his son plans to begin college this year in Colorado. Better note Springer’s location in pencil, not ink.

—Chuck Staresinic & Katie Hammer

THE WAY WE ARE
CLASS OF ’97

Sherri-Ann Burnett Bowie (MD ’97) is an instructor of medicine in Harvard Medical School. During her work on her MPH at Harvard, which she earned in 2005, Burnett Bowie noticed that often people with vitamin D deficiencies couldn’t process insulin as well as other people. So she is pursuing a study that will explore the connection between the two disorders. In 2005, she won the Massachusetts General Hospital Physician-Scientist Award and in 2006 she was a Chester Pierce Research Society Speaker at the hospital. Burnett Bowie says the problem-based learning sessions in medical school were great preparation for her work in endocrinology.

Pitt also prepared Devin Brown (MD ’97) for her career at the University of Michigan as a physician-scientist. As medical students, Brown and classmate Teresa Smith (née Jacobs, MD ’97) investigated the prevalence of primitive reflexes in healthy young adults to aid clinical evaluations of neurological disease. These infantile reflexes do not typically persist into adulthood, unlike, say, the sneeze reflex. But they are common in patients with frontal lobe lesions, schizophrenia, and Alzheimer’s disease. In 1998, the duo published their paper in Neurology with the help of former Pitt neurologist Laurie Knepper (MD ’85). Today as an assistant professor of neurology, Brown studies sleep apnea in stroke patients.

As the training director of the Office of Critical Event Preparedness and Response and assistant professor of emergency medicine at Johns Hopkins University, Ed Hsu (MD ’97) travels throughout the world evaluating medicine and public health problems in disaster-prone areas.

Hsu has worked with physicians and healthcare professionals in many nations, training doctors to handle medical situations following emergencies.

One month after classmate Brian Klatt (MD ’97) completed his tour as an attending orthopaedic surgeon in the U.S. Air Force, he visited Nepal and met some of Hsu’s colleagues who were helping the Nepalese plan for emergency care during earthquakes. Klatt served for five months in a field hospital at Camp Anaconda in Balad, Iraq, north of Baghdad, where he stabilized U.S. soldiers for transport to Germany and performed surgeries for Iraqis. During that time, though there were only three orthopaedists at the camp, more than half of the 1,200 surgeries the doctors performed were orthopaedic.

Klatt now works as a fellow in adult reconstruction at Thomas Jefferson University in Philadelphia. When we spoke with him, he was organizing his class’s events for Medical Alumni Weekend. —MH
**ROBERT BASFORD**  
AUG. 21, 1923–MAR. 11, 2007

Robert Basford enjoyed life as a scientist so much that it would surprise many who knew him to learn that his formal education nearly came to an end after high school. The North Dakota native told his students that he danced in the street for coins during the Great Depression. As a young man, he was an office manager before starting college. He received his PhD from the University of Washington in 1951 and spent five years on fellowships at the University of Wisconsin, Madison.

His career at the University of Pittsburgh School of Medicine began in 1958, when he joined what was then the Department of Biochemistry. Students and fellows remember him as a hands-on scientist who never hesitated to do the hard work himself or to give credit where credit was due. He was an avid cook and gardener who, with his wife, Carol Phebus-Basford (MD ’68), once invited his lab group over to see his night-blooming cactus. He made important contributions to understanding metabolism in the immune system and in the brain. He was acting chair of his department for four years, beginning in 1976, and retired as an emeritus professor in 1993.

—Chuck Staresinic

**ANDREW KEVERLINE**  
APR. 13, 1974–JAN. 22, 2007

Andrew Keverline was admired as the charismatic doctor who returned from the city to take over his dad’s ophthalmic practice following the elder Keverline’s death in 2002. Then Andrew Keverline (MD ’00, Res ’04) died this winter in a snowmobile accident in northwestern Pennsylvania. He was 32 years old.

Keverline was the fourth in his family to graduate from Pitt’s School of Medicine. He followed his father, Paul Keverline (MD ’69), brother Michael Keverline (MD ’97, Res ’01), and sister-in-law Sharon Keverline (MD ’97, Res ’01).

“Andy’s dream was always to go back and practice with our dad,” said Michael Keverline. Their father died one year before that could happen.

“He could have gone anywhere after residency. But he went back [to Warren] nine months after Dad died. Andy was fiercely loyal, and he had a strong sense of responsibility.”

Keverline is survived by his wife and two children, ages 3 and 4. —CS

**JAMES A. MAGOVERN**  
JUNE 8, 1954–MAR. 17, 2007

When James Magovern (MD ’80) was diagnosed with renal cancer in 2003, he put his surgical practice on hold to devote time to his research and his family. Magovern was the principal investigator on a National Institutes of Health study of a left ventricular device. He was also director of cardiac surgery research at Allegheny General Hospital and surgical director of the hospital’s Gerald R. McGinnis Cardiovascular Institute. Two of his research papers were in press at the time of his death. The father of four hails from an esteemed medical family. His father, George Magovern, was an early leader in developing artificial heart valves. Brother George Jr. received his MD from Pitt in 1978. Daughter Megan is currently in medical school. —CS

**CAMPBELL MOSES**  
FEB. 12, 1917–FEB. 11, 2007

A planned birthday party for Campbell Moses (MD ’41) suddenly became a memorial service, but it remained a celebration of his life. Moses died February 11, one day before his 90th birthday.

Moses earned his undergraduate and medical degrees at the University of Pittsburgh. He was a researcher who took part in the clinical trials of Jonas Salk’s polio vaccine and an associate professor of physiology and pharmacology. He directed and helped build the Addison H. Gibson Laboratory, which re-established live animal research at Pitt.

Moses left Pittsburgh for New York City in 1967 and became the medical director of the American Heart Association. Peers called Moses a gifted communicator and innovative medical educator who used film as an educational tool as early as 1949. After leaving the association in 1973, he was senior vice president for medical services at Medicus, a medical communications agency. He was an enthusiastic Manhattanite, frequently walking his adopted city and reveling in the many restaurants, cafes, and neighborhood shops where he was known by name.

Among the fond memorial service remembrances from his four children was a thank-you for demonstrating how to live a “principled and ethical life” and for “trying hard” to teach a son how to tie a bow tie. One of his 12 grandchildren added, “I am grateful you weren’t afraid to roll around on the floor and be silly. Thank you for keeping tetanus shots in your freezer.” —CS

**IN MEMORIAM**

<table>
<thead>
<tr>
<th>’40s</th>
<th>’50s</th>
<th>’60s</th>
</tr>
</thead>
</table>
| ALFRED R. CONTI  
MD ’44  
MAR. 10, 2007 | JAMES C. FRIES  
MD ’50  
JAN. 16, 2007 | HOWARD B. EISEN  
MD ’60  
MAR. 12, 2007 |
| ROBERT E. JOHNSTON  
MD ’46  
DEC. 31, 2;006 | RICHARD W. ZIMMERMAN  
RES ’57  
JAN. 30, 2007 | ROBERT H. BROUGHER  
MD ’61  
NOV. 21, 2006 |
| KENNETH KOST  
MD ’59  
MAR. 28, 2007 | ROY E. BOHL  
MD ’62  
OCT. 2, 2006 | BERNARD I. COHEN  
MD ’64  
JAN. 26, 2007 |

38 P I T T M E D
M ichael Grever (MD ’71, Res ’74) has learned that believing in second chances can pay off. An experimental drug he championed that once seemed ineffective now shows promise for leukemia patients.

Grever, who also received his undergraduate chemistry degree from Pitt and was recognized recently as one of the University’s Legacy Laureates, was a full professor in the Department of Internal Medicine at Ohio State University in the 1980s. There, he ran some of the first clinical trials of new cancer drugs. He would receive drugs from the National Institutes of Health (NIH) with instructions. His job was to determine their efficacy and to evaluate, when something went wrong, whether it was because of the new therapy or the underlying disease. Later, at the National Cancer Institute (NCI), he learned how the instructions were written. In 1989, Grever became deputy director of the NCI’s Division of Cancer Treatment and Diagnosis.

Grever eventually directed the institute’s drug discovery and drug development programs for cancer and AIDS. His team cracked open the molecular biology of exotic new compounds in search of targeted cancer therapies. They brought the most promising ones forward through animal studies until they were ready for clinical trials.

“As a result, we put about 19 to 21 new therapies into patients with cancer or AIDS,” he says, including pentostatin and fludarabine.

In the early 1990s, Grever and colleagues at the NCI began looking at a drug called flavopiridol as a treatment for chronic lymphocytic leukemia (CLL). In the Petri dish, it was a winner. There was a lot of excitement about moving it into Phase I testing in humans. When they tried it in patients, however, it bombed.

“It didn’t do anything,” says Grever. “It just produced diarrhea, and that wasn’t a very attractive side effect.” These disappointing results were repeated across the United States and in Europe. Before long, the drug company decided to drop the project, and the NIH began to lose interest, too. But Grever wanted an explanation.

In the lab, his team took human leukemia cells suspended in the patient’s own plasma and figured out how much drug was needed to kill the cancer cells. It took a much higher concentration of drug than anyone had thought it would. Why? The original lab tests used fetal calf serum, because human plasma is prohibitively expensive. Most of the drug was bound to human plasma protein and unavailable for killing cancer—something that hardly happened at all in calf serum.

Grever personally lobbied the NIH and the drug company to test flavopiridol again with different dosages and a new schedule of drug administration. These studies were conducted in his research laboratory at Johns Hopkins University. Shortly thereafter, he was back at Ohio State as chair of internal medicine—a position where he could make the drug a priority. In clinical trials, Grever says, the drug “was so effective that, for a while, it was killing the leukemic cells too fast. We went to the FDA, and they said, ‘Well, you can’t give up on this, because it’s very promising.’”

In fact, the rapid destruction of a large number of cancer cells can cause a major problem, because the body must clean up the mess and the toxic byproducts. Grever hopes flavopiridol can be used in combination with other proven leukemia drugs to achieve complete remission. He and colleagues reported the latest news on flavopiridol this January in the journal Blood, but there will soon be more. They have a Phase II study in CLL patients under way, and other institutions are trying to reproduce their work.

“We’ve treated over 80 patients,” Grever says, “and this is all holding up. This is going to be one of the most active agents in the treatment of this disease.”
It was a dark and stormy summer at Lord Byron’s Lake Geneva home. Seeking a playful literary distraction for his guests—the soon-to-be-wed Mary and Percy Shelley as well as his physician, John Polidori—Byron challenged them each to pen a horror story to share. The following spring, in May 1817, Mary Shelley finished Frankenstein; or, The Modern Prometheus, which many consider the first science fiction novel. It was published anonymously the next year. (For his horror story challenge, Byron himself wrote a bit about the vampire legends he had heard in his travels, inspiring Polidori to later write The Vampyre, the first book in the romantic vampire genre.)

Shelley had a vivid imagination, but medical science also contributed to her story. A National Library of Medicine exhibition reports: Scientists and physicians of her time, tantalized by the elusive boundary between life and death, probed it through experiments with lower organisms, human anatomical studies, attempts to resuscitate drowning victims, and experiments using electricity to restore life to the recently dead.
CALENDAR
OF SPECIAL INTEREST TO ALUMNI AND FRIENDS

For information on an event, unless otherwise noted, contact the Medical Alumni Association: 1-877-MED-ALUM, 412-648-9090, or medalum@medschool.pitt.edu.

MEDICAL ALUMNI WEEKEND 2007
MAY 18–20
Reunion Classes:
1947  1952
1957  1962
1967  1972
1977  1982
1987  1992
1997

SENIOR CLASS LUNCHEON
MAY 18
11 a.m.
Soldiers & Sailors Memorial Hall

PITT MED REUNION
LEMONADE SOCIAL
MAY 18
1:15 p.m.
Schenley Park Visitor Center
RSVP to:
Victoria Shaver
svictoria@pmhsf.org
412-802-8319

SCHOLARSHIP APPRECIATION TEA
MAY 18
3:30 p.m.
William Pitt Union Lower Lounge

ALUMNI WEEKEND OPENING RECEPTION
MAY 18
5:30 p.m.
Holiday Inn Select University Center

CLASSES OF 1957 & 1972 DINNERS
MAY 18
7 p.m.
Pittsburgh Athletic Association

SCOPE AND SCALPEL’S “DESPERATE HOUSESTAFF”
MAY 18 & 19
7:30 p.m.
The Antonian Theatre
Carlow University
For information: www.scopeandscalpel.org

CME LECTURE
MAY 19
8:30 a.m.
M. Michael Barmada, PhD, Speaker
“Genomic Medicine: From the Human Genome Project to Personalized Medicine”
Scaife Hall

ALUMNI BRUNCH & MEDICAL SCHOOL TOUR
MAY 19
10 a.m.
Scaife Hall

REUNION GALA
MAY 19
6 p.m.
Senator John Heinz History Center

SENIOR CLASS PICNIC
MAY 20
Noon
Cathedral of Learning Lawn

CLASS OF 2007 COMPLENEMENT
MAY 21
10 a.m.
Sherwin Nuland, MD, Speaker
Carnegie Music Hall

SIMMONS LECTURE
MAY 23
8 a.m.
John C. Alverdy, MD, Speaker
Room S100
Starzl Biomedical Science Tower
For information: www.surgery@upmc.edu

TO FIND OUT WHAT ELSE IS HAPPENING AT THE MEDICAL SCHOOL, GO TO www.health.pitt.edu
YOU COULD WATCH THE GRASS GROW

But it might be time to take action to grow your legacy at the School of Medicine. Your support is needed. Help sow the seeds of success for future generations of medical students. In addition to contributing to your alma mater, you could establish a gift that would provide you (and/or a loved one) with an annual stream of income for life as well as tax advantages. There are many giving opportunities that could benefit both the school and you.

For information, please contact: Kathleen Helling, Director of Planned Giving, at 412-647-4220 or at hkathleen@pmhsf.org.

PHOTO COURTESY J. MIKSCH. ASSOCIATE EDITOR JOE MIKSCH’S GRANDMOTHER AND GRANDFATHER MARGARET AND HENRY MIKSCH (RIGHT) WITH FRIENDS. PHOTO CIRCA 1940.