UP FOR AIR
WHAT ANDEAN MOUNTAIN DWELLERS TELL US ABOUT TUMOR GROWTH
WHO WAS YOUR BEST TEACHER?  
If we would be negligent not to mention her nephrology notes, or lax not to wax on his elucidation of lymph, let us know. For an upcoming story, we’re looking for the greatest teachers ever to assume the lectern at the University of Pittsburgh School of Medicine. Send us your votes and anecdotes.

NOT-SO-OLD DOCS, NOT-SO-NEW TRICKS  
Robert A. Zolten, MD ’64, writes that he is the “bewildered young man” on page 40 of the July issue. Being bewildered and all, he doesn’t recall much about the circumstances of the photo, just that he was on the yearbook staff and they “took a lot of silly pictures for that book.” He sent us an updated photo:

1963

2000

GIVING FLOREY ET AL. THEIR DUE  
This just in to our Department of Amplification:

A minor editing change in “Quick On Their Feet” (July 2000) minimized the contributions of Howard Florey and his team at Oxford University in the wartime development of penicillin. Although Alexander Fleming first discovered penicillin’s antibiotic properties in 1929, reporting that an errant mold blew into an open lab window, settled on a forgotten petri dish and killed its bacterial contents, it was Florey’s group that actually developed it into a curative “miracle drug,” and Fleming always generously gave them credit. Their feat won the Nobel Prize for Florey, Ernst Chain, and Edward Abraham. Chain and Abraham were knighted; Florey became a life peer.

Chain deciphered penicillin’s molecular structure just over 60 years ago; Abraham and the biologist Norman Heatley devised a way to cultivate it in flat containers (first using hospital bedpans). Heatley conducted the first hugely successful animal experiments, in 1940. A few months later, penicillin was tried for the first time on a human patient, an Oxford police constable suffering from a horrifying staphylococcal and streptococcal infected wound. Although the infection was checked, the patient died when the meager supply of the new substance ran out.

The Oxford group was also responsible for the first successful use of penicillin on an American patient. Anne Miller, 32, wife of a Yale administrator, was comatose, with fevers spiking to 107 and so riddled with infection that the bacteria count entry on her hospital chart used the symbol for infinity. Yale neurophysiologist John Fulton, a close friend and colleague of Florey’s, asked his help. Fortunately Heatley was in New Jersey helping Merck and Co. set up a penicillin manufacturing line and delivered a small amount of the precious medicine to New Haven. At 3:30 p.m. one Saturday Anne Miller received her first injection of 850 units—an infinitesimal amount by today’s standards. (The maximum amount she received was calculated at 35,000 units.) By Sunday morning her temperature was normal, and she sat up and ate a hearty breakfast. Ms. Miller lived to the age of 92 and died only last fall.

The first supplies of penicillin were reserved for the military. But by late 1944 (as Pitt med students soon learned) there was enough for civilian patients, too.

By the way, just east of Pitt, at its old athletic rival campus Penn State, in 1935 a young graduate student, Roger Reed, sought approval for research into pharmaceutical applications for Fleming’s discovery. His faculty advisor convinced him there was no future in it.

In a place of honor in my living room stands one of the original penicillin vessels, a flat, oblong, spouted ceramic container designed by Heatley and manufactured in the famous Staffordshire potteries. A battalion of unsung “penicillin girls” cultivated and poured off the lifesaving stuff.

Heatley resurrected it from an outbuilding behind his cottage near Oxford and presented it to me. This wiry, cheerful man was not knighted and never received a shilling for his contribution, but was intensely—and understandably—proud of his and the Florey group’s work.

Ed Kiester Jr.
Menlo Park, California

NOBLEST KNOBIL

I enjoyed your tribute to Dr. Knobil, who taught me physiology at Pitt and my son Joel physiology at UT Houston Medical. He was a grand guy, and I think that I am an endocrinologist because of his influences.

Fred E. Ciarciochi, MD ’69
Duncanville, Texas
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She beat Linus Pauling to the punch, and that was after she and Michaelis set the stage for a new era in biochemistry.
So, what was her name again?
BY REBECCA SKLOOT

Look Again
The often tragic world of familial mood disorder is unmasked.
Neuroimaging tells us depressed brains are biologically different.
BY EDWIN KIESTER JR.

As Eyes Adjust to the Darkness
There's a stipend, but the pay isn't what this summer job is about.
The chance to conduct research with a faculty mentor is priceless.
BY REBECCA SKLOOT
Members of our Class of 2004 are settling in, beginning the grand journey toward becoming physicians. It’s a journey that will lead to uncharted territory for them, and the rest of us as well. For centuries, medicine has been population based. We give all adults the same dose of penicillin, and we consider everyone equally vulnerable to radon exposure. Yet human beings are not uniform in their ability to absorb and metabolize drugs, nor in their susceptibility to disease, to name just two of the important ways in which we differ.

In the wake of the Human Genome Project—as we undertake the daunting challenge of illuminating the structure, function, and interactions of proteins (the ultimate expression of our 100,000 genes)—basic research will restock the physician’s “black bag.” We will be equipped for prevention, diagnosis, and treatment as never before. Understanding a patient’s genetic makeup will allow us to select the drugs most effective for a particular form of a disease (for example, the many variants of lymphoma) as well as the appropriate dose for optimal therapy and minimal risk. Along the way, we should not lose sight of the enormous roles that environment, behavior, and diet play in affecting our lives, albeit within the context of our genetic heritages.

This new frontier also will lead us to a range of profound ethical dilemmas, many of which we have considered before, yet only sporadically and for limited sets of people. (Consider how you go about defining “preexisting condition” in an era when a risk can be identified genetically at birth—long before one presents clinical symptoms.) How do we balance individual privacy and freedoms with society’s desire to advance public health and reduce the economic burden of disease? We need to be exceedingly sophisticated, sensitive, and fair-minded when dealing with these extraordinarily challenging issues. It will be effort and energy well spent.

Advances in genetics and its concomitants (molecular, structural, cell, developmental, and computational biology) are auspicious for our quality of life in other areas as well: Consider the economic promise. The biotech industry now employs 150,000 nationally and generates $21 billion annually. More than 270 million people have been treated with the 100 biotech products available. Though there are about 300 known molecular targets for drugs in our cells, it’s thought there are as many as 5,000 to 10,000. Each of these targets will fuel biotechnology-driven drug development; and in terms of industry growth, my bet is biotech will dwarf e-commerce, given time. As this industry grows in southwestern Pennsylvania, it could likely prove tantamount to what steel once meant here.

At Pitt, we are positioning ourselves to lead the way. Our knowledge of the human genome will revolutionize the practice of medicine, but this knowledge is even more important: Genetics has much to teach us about our relationship to life on this planet, the astonishing degree of genomic universality in all living creatures, the variations that contribute to our diversity and survival—as well as to disease—and the uniqueness to which each of us lays claim. Few other discoveries have been more important, in this or any other time.

Arthur S. Levine, MD
Senior Vice Chancellor for the Health Sciences
Dean, School of Medicine
Your PET Is in My CT

Sometimes a picture is worth more than a thousand words. This image of laryngeal cancer comes from the University of Pittsburgh and UPMC Health System's one-of-a-kind PET/CT scanner. Computed tomography (CT) scans alone of the cancer would show a fuzzy gray mass. A CT scan can distort images of tissue that has already been radiated or operated on, and it cannot detect early stage cancers. Positron emission tomography (PET) technology shows the living cancer as a bright orange glow, courtesy of a radiopharmaceutical that triggers a release of gamma rays in tumorous tissue. Yet PET scans alone don’t show where tumors begin and end, images that are necessary for precise biopsies or other surgery. By combining PET and CT, says Carolyn Cidis Meltzer, associate professor of radiology and psychiatry and medical director of the PET Facility, physicians can localize cancers with great success. After two years of operation, Meltzer says the PET/CT scanner continues to draw international visitors to Pitt. The 46th Annual Meeting of the Society of Nuclear Medicine chose this scan as its Image of the Year. —ET

FOOTNOTE

Many admire Henry Bahnson, the distinguished Pitt professor of surgery. Well, he has his own heroes, including Howard Levy, who apparently blows a harmonica like nobody’s business. Bahnson studied the musician’s technique (anatomically and physiologically), then developed the Bahnson Overblow Harmonica. The first batch has sold out.
Faculty Snapshots

SOME RECENT FACULTY ENDEAVORS AND KUDOS:

A recipient of a Charles E. Culpeper Scholarship, Charleen T. Chu plans to continue her research involving cellular mechanisms that may promote neurodegeneration in regard to Parkinson's disease. In addition to Chu, an assistant professor of pathology and ophthalmology, the Rockefeller Brothers Fund awarded Culpeper Scholarships to three researchers from the faculties of Cornell University, Stanford University, and Washington University.

Shi-Yuan Cheng's brain tumor research has not gone unnoticed. The assistant professor of pathology has been named a 2000 Kimmel Scholar by the Sidney Kimmel Foundation for Cancer Research. The award provides Cheng with $200,000 during the next two years, which will allow him to continue his research that, ultimately, could lead to a breakthrough for blocking tumor growth.

In the May issue of Nature Medicine, senior author Stephen Strom states that life-threatening consequences are linked to an anticancer compound that had been slated for clinical trials. The associate professor of pathology and Burroughs Wellcome Visiting Professor determined that the compound (TNF-related, apoptosis-inducing ligand) causes catastrophic damage to human liver cells, though it was harmless to mice in preclinical testing.

A $6 million National Institutes of Health renewal grant was bestowed upon the University's Brain Trauma Research Center; it allows researchers to continue exploring why some patients recover better than others from brain swelling following head injuries. During the five-year span of the grant, researchers also hope to illuminate the role drugs play in treating brain injuries.

Bartley P. Griffith is the principal investigator in Pittsburgh of a multicenter study that may eliminate the need for donor blood during surgery. The perflubron emulsion being tested by the professor of surgery may allow surgeons to remove significant amounts of blood from patients before they undergo a procedure and also permit patients to bleed beyond the point at which a transfusion is normally required. The hope is that the need for donor blood during surgery will be reduced or entirely eliminated. Forty centers are participating in this international trial.
So, there you are, one of about 1,500 faculty members at the University of Pittsburgh School of Medicine, and you think you might be on the brink of a treatment for (fill in the blank). If only you better understood the pathogenesis of (fill in the blank). And there must be someone who would be good at designing something that would (blankety-blank). How do you find the right collaborators?

Sometimes word of mouth takes you only so far. That’s why—as part of the Pittsburgh Integrated Advanced Information Management Systems Program—Pitt’s Center for Biomedical Informatics, Health Sciences Library System, and Office of Research—Health Sciences are creating the Faculty Research Interests web site. It relies on the National Library of Medicine’s MEDLINE keyword system to help make sense of the University’s small universe of information.

Developers say the site also will allow administrators to target announcements about funding opportunities, help students and postdocs find appropriate labs in which to train, and enable scientists from other organizations to find research partners. The site was launched this summer at the School of Medicine; developers will roll in other health sciences faculty information starting this fall.

—EL

For more information:
http://www.cbmi.upmc.edu/~frip/index.html

No Spilt Blood

Transfusionless Surgery | By Celeste Kimbrough

Only flesh with its soul—its blood—you must not eat.

Genesis 9:4 is a primary reason Jehovah’s Witnesses refuse blood transfusions. Each year, one-half million followers of the religion assert that spilt blood may not be reintroduced into the body under any circumstances. To aid Jehovah’s Witnesses in need of heart surgery, Brack Hattler, professor of surgery at the School of Medicine, has established the Bloodless Cardiac Surgery Program, in which transfusions are not only unnecessary, but also prohibited.

Here’s how the approach works. Before surgery, the patient and surgeon forge a contract. The contract releases a surgeon from liability and prevents the surgeon from transfusing blood even under life-threatening conditions. However, by a rigorous screening of surgery candidates, the likelihood of an emergency decreases markedly. Hematologists ensure that a candidate possesses a well-orchestrated clotting system and is free of blood thinners. Before the procedure, the patient takes Epogen to stimulate red blood cell production. (Epogen is administered until the hemoglobin count reaches a level of 15 or the hematocrit 50.) The surgery lasts about an hour longer than traditional procedures because surgeons must seal off broken capillaries using a laser coagulator.

The program took shape this year, but throughout the past 10 years, Hattler has performed more than 100 transfusionless surgeries. Recovery time averages just one day longer.

The program plans to target areas with significant populations of Jehovah’s Witnesses, including the religion’s founding city, Pittsburgh. In the long run, Hattler envisions a much wider population benefiting: “In general, most patients would prefer not to be transfused. This technology could potentially be the most desirable option for the general population and eventually become a standard in surgery.”

Flashback

This debate has bridged centuries. Found in the 1946 Hippocratican, re proposed socialization of medicine:

“Of such is the peculiar political philosophy of practically all the social planners who hope to achieve their socialistic ambitions through federal legislation—legislation which would, in a few short years... dry up the private funds and local tax sources which now provide for hospitals and medical schools...”

—Walter F. Donaldson

1946 Editor Pennsylvania Medical Journal

Word of Web

A Site that Marries Research Interests

S
Appointments

A FEW OF THE WELCOME ADDITIONS TO THE SCHOOL OF MEDICINE’S FACULTY:
Andrew M. Yeager found himself featured in *Time* magazine after performing a stem cell transplant that effectively cured one of his young patients of sickle cell anemia. (Stem cell transplantation involves the replacement of malfunctioning or cancerous cells with precursors of normal, healthy cells, i.e., stem cells.) Yeager performed this pioneering procedure while at Emory University in Atlanta, Georgia, as a professor in the Departments of Medicine and Pediatrics. He has joined Pitt's Departments of Medicine and Pediatrics and will direct a stem cell transplantation program here. He intends to further his research in stem cell transplantation for diseases such as leukemia, lymphoma, scleroderma, multiple sclerosis, and systemic lupus erythematosus.

Diagnosis and treatment of such diverse disorders as Parkinson’s disease, spinal cord injury, stroke, obsessive-compulsive disorder, and autism all relate to the research of Peter L. Strick, who is now a professor in the Departments of Neurobiology and Psychiatry. Strick—most recently the George Perkins Professor of Neurosurgery at the State University of New York Upstate Medical University in Syracuse—focuses on the structure and functions of brain regions concerned with the control of movement and cognition. Strick is codirector of the Center for the Neural Basis of Cognition.

Ross Zafonte has been appointed chair of the physical medicine and rehabilitation department. He is particularly interested in the rehabilitation of patients with traumatic brain injuries. His research centers on promoting recovery by employing a combination of medications and therapy. Through his work, he hopes to improve the accuracy of prognoses for patients. Prior to coming to Pitt, he was the interim chair of the physical medicine and rehabilitation department at Wayne State University in Detroit, Michigan. —RM

**T H E Y W O N ’ T C A T C H A C H I L L**
The afternoon of August 6 was hot and muggy—certainly no need to bundle up. Yet among the Class of 2004, seated 10 rows deep in Scaife Hall, not one minded wearing a coat. A White Coat. After he was formally “coated” at the Medical Alumni Association sponsored ceremony, Leon McCrea, MD ’04, (left) talks with Brian K. McNeil, MD ’01.
T

here are many paths to medical school. Some are tra-

ditional. Some are nontraditional. Some appear, at

first, preposterous. Sarah Clark Grudberg, MD ’99,

chose the preposterous route.

Sure, she received good grades at a “typical big suburban

high school” near her Woodbridge, Connecticut, home. And

she was accepted to Yale University, as were her father before

and her four older brothers, too. Smart family. With one

caveat. “I did not do well at Yale,” admits the history major.

“Not at all! I had a fantastic, wonderful, happy time at Yale,

most of it outside the classroom.”

Sounds like a fun way to approach school. Sounds like a

way to wind up as a hostess at Pizzeria Uno. “Do you prefer

the smoking or nonsmoking section?” was the daily question

for the Ivy League graduate with a 2.9 GPA.

“I definitely didn’t have focus,” she says.

Her hostess stint lasted only a few months. Then she and

a good friend traveled to Thailand, where they spent six

months soaking up the culture while teaching English. Why

Thailand? “It was the decision of an unsophisticated 22-year-

old brain,” she recalls. “My friend and I thought, ‘Oh, every-

one goes to Europe. Why don’t we go to someplace interest-

ing, like Southeast Asia?’”

She moved to the Boston area and joined Lotus Inc.
in an administrative position. Three years later, she

was a “quality assurance engineer,” and even

though she liked the company, she says, “It’s not

that compelling to me to make a spreadsheet.”

Medicine, at last, entered the picture. “I had done

enough hanging out to know that I wanted some-

thing more,” she says.

Off to night school she went at a “fantastic”

public access program through Harvard University.

She started with chemistry and did well: “I loved it,

and I showed myself: I can do this.” Two years later she

had completed all the courses necessary to apply to

medical school. Then came the MCATs. The results

(which she politely declined to reveal publicly)

placed her in the upper echelon of prospective med-

ical school students.

Upon her graduation last year from the University of

Pittsburgh School of Medicine, she received the

Humanism in Medicine Award from the Health Care

Foundation of New Jersey. The award recognizes a stu-

dent who “consistently demonstrates compassion and

empathy in the delivery of care to patients; illustrates

professional behavior by example; shows respect for

everyone she comes in contact with . . . [and] shows

good rapport with patients.”

Grudberg—slightly more than a decade removed

from her days as a restaurant hostess—is in her

second year of the internal medicine residency at

Brigham and Women’s Hospital in Boston. What

were the odds? —RM

“Alumni Checkup with Sarah Clark Grudberg

At the Pittsburgh University Medical Center the investigation continues into the murder of surgical resident Kevin Hoover.”

—Excerpt from Abra Cadaver

Physician James Tucker uses a thinly veiled academic medical center and a med school we all know as the backdrop for his medical/magic suspense series: Abra Cadaver, Hocus Corpus, and his latest book, Tragic Wand, released this month. Tucker did his residency at Children’s Hospital of Pittsburgh, so his hero, Jack Merlin, MD, is no stranger to Scaife Hall, the Original Hot Dog Shop, among other Oakland—excuse the pun—haunts. —RM
Researchers in 1972 chose the Greek word suggesting falling leaves, apoptosis, to describe a newly characterized morphology of programmed cell death. It's a fitting name on many different levels, says Xiao-Ming Yin, School of Medicine assistant professor of pathology and an MD/PhD. Leaves die and fall intact, and cells killed by apoptosis shrink with nuclei intact. This is not a violent death compared with what often happens in cells killed by inflammation or injury—they are more likely to explode. And both apoptosis and a tree's autumnal blush mean development as well as death. Leaf death makes room for spring buds; cellular suicide allows fetal fingers and toes to separate and helps tadpoles shed their tails.
Death is as important as growth, says Yin, whose lab is one of several at the University of Pittsburgh seeking to uncover the mysteries of apoptosis. His research into a molecule that triggers apoptosis might translate into, for example, a more effective means of killing tumors or preventing certain autoimmune diseases and liver cell death due to disease.

Apoptosis, Yin notes, appears to follow one of two pathways, both of which can be associated with the pathogenesis of human disease.

A well understood pathway begins with the death receptor Fas/TNF-R1, which is tied to a host of diseases. When Fas/TNF-R1 is activated on a cell, it sets off a chain reaction that ends in the cell’s destroying itself. A more mysterious pathway involves mitochondria that can be activated by radiation or other stimuli to release cytochrome c, a substance that causes a flood of caspase enzymes that hack apart DNA and kill the cell.

No one knows exactly how mitochondria go about releasing cytochrome c. Many, however, believe that studying a molecule called “Bid”—which was first cloned by Yin—could unlock those hidden mechanisms and pave the way for more detailed study of the role apoptosis plays in disease. Yin is trying to figure out, for example, whether Bid enters the mitochondria and then creates a special pore that releases cytochrome c or whether it helps release it some other way.

He cloned the killer molecule four years ago. Then, in 1998, researchers at Harvard University and the University of Texas cloned Bid again, revealing more of its characteristics. This helped Yin and his colleagues pinpoint where Bid stepped in to facilitate the apoptotic chain reaction.

The molecule continues to intrigue those studying the intricate biochemistry of a range of diseases. Although it is one of four molecules—family members are Bax, Bak, and Noxa—believed to play similar apoptotic roles, Bid is the only molecule with a defined trigger. Yin’s earlier research helped scientists focus on Bid. His work determined that Bid links the two cell death pathways, with the activated death receptor Fas/TNF-R1 releasing a caspase enzyme that triggers Bid to move to the mitochondria and complete its work.

Using knock-out, or genetically altered, mice, Yin also determined that Bid is important in hepatic diseases. Mice without Bid molecules proved resistant to apoptosis when injected with an antibody directed against Fas whose effects mimic viral hepatitis. Wild type mice—i.e., mice that were not genetically altered and that, presumably, still had Bid molecules—died. It appears the antibody was ineffective without Bid, implicating the molecule in the executioner’s role.

In addition to unveiling its hidden mechanisms, Yin wants to find out why Bid is important to apoptotic events in hepatocytes and in neuronal cell death after stroke.

This sort of investigation could help scientists elucidate the apoptotic chain reactions in other disease models, too, he believes.

It looks like understanding how this executioner works may save lives down the road.

FOR MORE INFORMATION: http://path.upmc.edu/people/faculty/yin.html
VTAs, though rarer, are the typical path to ventricular fibrillation leading to sudden death.

Shusterman didn't always speak with such conviction. He remembers a day not so long ago, somewhere in the blur of 1996, when he was mired in data and, he thought, getting nowhere. In 1995, Shusterman, who is from Novosibirsk, Russia, had accepted a postdoctoral fellowship with the Cardiovascular Institute's Kelley Anderson. Anderson was helping to wrap up a huge multi-year, multicenter clinical trial led by the University of Utah in Salt Lake City. The electrophysiologic study tracked 487 patients who had experienced VTAs, monitoring them in periodic 24-hour intervals using a device that continuously records ECG data. Shusterman, who has a PhD in artificial intelligence as well as an MD, was eager to mine the data. He had developed mathematical methods for analyzing how the nervous system controls heart and blood vessel functions; and both he and Anderson thought it would be fruitful for him to apply those methods to the Utah study.

“Everyone understood that the data were unique,” says Shusterman. Once he got settled in Pittsburgh, Shusterman used spectral analysis to examine frequency patterns from electrocardiograph signals, applied various analytic techniques among patient groups, and gleaned a few interesting things from the data, but nothing that allowed him to predict arrhythmia. This was a mess, he began to think.

“I doubted it was possible to predict arrhythmia accurately—others had tried and were not successful,” he says.

“Finally I said, ‘Maybe I’m missing something. Let’s forget everything that I learned or used before.’”

Not so long after Shusterman shifted his mind-set, something occurred to him. He had seen enough data to realize that everyone’s heartbeat has a unique pattern, just as everyone’s voice has a unique pitch. So all this analyzing of patient groups would never allow him to see which electrophysiologic events might portend arrhythmia. However, if he could identify individual patterns of heart rate, then his methods would allow him to pinpoint abnormalities and, perhaps, predict when those abnormalities might take place.

Bingo. He was finally on the right track.

He and his colleagues went back to the Utah study and decoded individual heart patterns—using 24-hour ECG recordings from 60 patients when they experienced VTAs and the control recordings from the same patients when they did not have VTAs. Applying pattern recognition techniques adapted from AI methods, he was able to see that persistent abnormalities in the heart-beat pattern occurred in the hours before an arrhythmia. This could facilitate an accumulation of disturbances in waves of electrical activation spreading throughout the heart—which appeared to trigger the arrhythmia. From there, Shusterman was able to develop an algorithm to predict arrhythmia up to eight hours before its onset. Together with Pitt’s Barry London, he tested the process on arrhythmia-prone mouse models that Arthur Feldman of the Cardiovascular Institute had developed.

Just as he’d hoped, Shusterman was able to predict arrhythmias in the mice.

So far, Shusterman’s technique has been applied by taking ECGs and running his software to analyze them. He is collaborating now with Guidant Corporation outside Minneapolis, Minnesota, to insert the software and a miniature computer into defibrillators to allow real-time analysis and detection. The technology could be applied inexpensively to many cardiac monitoring situations. It could be used in devices such as pacemakers and in hospital monitors connected to patients at their bedside; or physicians could use it to analyze periodic ECGs.

All this doesn’t exactly mean a sudden death for sudden cardiac death, though its downfall seems to be looming.

Once Shusterman gets past what he calls the ‘organizational’ challenges of large clinical trials and puts his invention to broad use, physicians who use this technology will be alerted to danger signs in their patients with histories of arrhythmia, enabling them to intervene as necessary.

Looking back at those days when he felt he was treading in a morass of data and getting nowhere, Shusterman notes, “Sometimes you have to disregard prior knowledge and concepts that blur your vision. It’s useful to look at the problem without prejudice.”

For every 3,000 baby boys, one is born with Duchenne muscular dystrophy (DMD). He looks and acts like other children: he cries, nurses, and smiles; learns to support his body, first head, then frame. But sometime between his third and seventh year, his muscles begin to deteriorate. If he can walk, each step becomes a forced, concentrated effort. If he runs, he propels himself forward with labored, waddling strides, his back arched and belly thrown forward to balance against his weakening pelvic muscles. He falls. Accidents grow more frequent. As early as his ninth birthday, braces may be his only hope for walking; and by about age 12, he will be confined to a wheelchair. Soon after, the muscles in his hands and arms will weaken, as will those that allow him to breathe. He will probably not live through his teens.

Muscular dystrophy is a family of disorders marked by slow muscular degeneration. The most common form, DMD, is caused by a mutation in the gene for dystrophin, a protein essential for muscle-cell membranes. Those with limb-girdle muscular dystrophy (LGMD) are born with a mutated gene for sarcoglycan, another muscle-cell membrane protein. (LGMD is much less common than DMD.) These mutations leave the body unable to produce a protein vital for muscle function. The price is something Xiao Xiao, assistant professor of molecular genetics and biochemistry, calls “leaky muscle cells.” Eventually muscles cease functioning as the body slowly replaces them with firm connective tissue. There is no approved treatment. But in Xiao’s lab, when he injects viral vectors with functional copies of these genes into animal models, protein levels rise to near normal, and the disease state vanishes.

Xiao works with the adeno-associated viral (AAV) vector, which offers the first hint at a treatment for patients with muscular dystrophy. It’s considered the safest vector—even in its natural state, AAV doesn’t cause human disease and is incapable of replicating without assistance from another virus. And Xiao is intimately familiar with it. AAV was developed by his Pitt PhD advisor, Jude Samulski, who isolated the virus and removed its viral genome to allow insertion of therapeutic genes.

The sarcoglycan gene, which Xiao hopes to use for treating LGMD, fits nicely into AAV, but the dystrophin gene is about 600 times too big. So Xiao created a minidystrophin gene, one with all the functional DNA it needs, and made it fit into an AAV vector. Then, in two studies, he injected these genes into the leg muscles of animal models. Both the LGMD and the DMD groups began producing normal levels of their missing protein and showed verifiable improvement. The LGMD study is furthest along. That collaboration with John Watchko, a Pitt professor of pediatrics, showed muscle force, which was 50 percent of normal prior to treatment, recovered to 97 percent.

Xiao is preparing for an LGMD clinical trial. He’s not sure how the turmoil over gene therapy will affect his plans, but he believes the AAV vector is a highly promising therapy and will also help safeguard his subjects’ health. He is determined to help those with MD—even if, along the way, each step becomes more labored as time progresses.
Bora Baysal and Joan Willett-Brozick found a mutation that causes paraganglioma tumors. That's causing a stir because it looks as if the same defect may encourage the growth of common cancers.
According to the clock on the laboratory wall, it’s 11 p.m. Besides that clock, there is only one other hint that the workday has long ago ended for most people. It’s the lone window across the room. From this vantage point on the 14th floor of the University of Pittsburgh’s Western Psychiatric Institute and Clinic, Fifth Avenue looms in the distance. The thoroughfare’s perpetual traffic has dwindled to an occasional PAT bus and nocturnal automobile.

But nobody bothers to peer out the lab window tonight. Nobody glances at the clock, either. Bora Baysal and Joan E. Willett-Brozick focus only on their data. They don’t like what they see.

They are searching for a genetic mutation within one single gene from a pool of what has been estimated to be 100,000 genes in the human genome. The search had been progressing well. Until now.

For Baysal, who today is an assistant professor of psychiatry and human genetics at Pitt, the search began in 1994, shortly after he left Ankara, Turkey, for Pittsburgh. His departure was the culmination of a career-altering decision. In 1988, he graduated from Gulhane Medical School in Ankara, and practiced medicine for two years as a family physician; but he found himself drawn to the "unknowns" of genetics, fascinated by the idea that answers to what makes one susceptible to certain conditions and diseases could be hidden away in the human genome. He began predoctoral training and received an international fellowship, which stipulated that he pursue his graduate education abroad. He decided on the University of Pittsburgh because, in large part, he had great respect for Robert E. Ferrell, who at the time chaired the Department of Human Genetics at the Graduate School of Public Health.

After settling in at the University, Baysal needed to choose a dissertation topic, although in his field, he points out, "choose" isn’t a totally appropriate word for selecting a project:

"It’s not something you can entirely determine yourself. It depends on patient material, so availability of family material is one of the most important factors directing your research. You find a very interesting genetic family and start your career."

That is how hereditary paraganglioma entered his life. His PhD advisor, Charles W. Richard III, had contact with several families located in Pennsylvania with this rare hereditary disorder.


cover story

with help from andean mountain dwellers,
an oxygen-sensing gene is linked to tumor growth

by robert mendelson

up for air

portrait photography | jim judkis
Researchers found that the frequency of the tumors increased for inhabitants of higher elevations.
For those with hereditary paraganglioma, tumors generally start appearing after the age of 30, sometimes on the head, but usually along the carotid bodies (the tiny neurovascular workers located on the carotid artery that help the body respire). By the time the patient is 60 years old, some sort of tumor presence is highly probable. It’s not a life-threatening disorder, although it may compress critical nerves and arteries in the neck, which can lead to health problems. Surgery in an advanced state is risky because of potential nerve damage and significant disfigurement of the head and neck. Tumors can grow as large as half a skull.

Richard’s access to several local families with the mutation was a boon to Baysal. “These genetic families,” he says, “are precious resources for gene mapping.”

He had his project.

Baysal wasn’t alone in his search. This genetic condition is most prevalent in the Netherlands, so Dutch researchers had been searching for the genetic mutation, too. Through Richard, Baysal established a collaboration with a Dutch group.

“The Dutch had crudely identified the gene location,” Baysal recalls.

On the basis of their research, he focused on approximately 500 genes.

“We elaborated on this mapping process, and for years we and the Dutch tried to narrow down the critical region further and further and further.”

The mapping process won’t be the pilot for a new television drama anytime soon. “This process is extremely boring,” he says. “All you do is obtain new families and analyze chromosomes of affected individuals to see if you can narrow down the location.”

He and Willett-Brozick, a laboratory researcher, systematically did this day after day, week after week, year after year. Usually 10 to 12 hours daily, Monday through Friday; more hours on Saturday and Sunday. No vacations. Few distractions for the bachelor, other than a two-mile, straight-line jogging course from his Shadyside home to his Oakland laboratory.

“Bora lives this stuff; it’s his life,” says Willett-Brozick, who conducted the gene-mapping experiments.

The hard work paid off. By the beginning of 1997, the search had been narrowed by Baysal to approximately 175 genes. More good news.

The Dutch had identified a specific region where they believed the mutated gene would be found; that region was located among the 175 genes still under Baysal’s scrutiny. It seemed they were on the right track. Seemed.
Baysal found a mutation that causes mitochondria to act as though they're in an oxygen-deprived environment. As a result, the tissue works overtime producing cells.

Baysal and Willett-Brozick continue to stare at the data. At each other. At the data again. It doesn't make sense.

Clearly, something is wrong. There can be only two explanations, reasons Willett-Brozick. It is a technical problem on Baysal's end, or else the Dutch haven't interpreted their data correctly.

Baysal finds no discrepancies in his data. At last they go home, the search narrowed no further. Tomorrow is no different. Or the next day. Or the next.

It's time for a lab meeting. Willett-Brozick, Baysal, and Richard talk. And, in the case of Baysal and Richard, they talk loudly. Very loudly. Willett-Brozick isn't surprised. In fact, she is used to it. “Charlie and Bora have really big hearts for science,” she says. “They just love it; they get very excited, and lungs to work harder so the body can adapt to lower oxygen levels. If you are in a continuously low oxygen environment, like the Indians living in high altitudes, this tissue keeps working and working and working and the number of cells increases and leads, eventually, to the Indians’ tumors.

“While there are hundreds of papers about carotid bodies and paragangliomas,” says Baysal, “I couldn't see anyone emphasizing the similarities: people with this genetic defect who lived in low altitudes experiencing the same kind of tumor that normally occurs in people living in high altitudes.”

From this “coincidence” springs Baysal’s theory: The problem for hereditary paraganglioma might be a defect in oxygen sensing.

Immediately, Baysal and Willett-Brozick scan those genes in the remaining A megabase target region (i.e., approximately 10 genes) to find out whether they might be involved in oxygen sensing. They find one. Next, they need to run what’s known as a single stranded conformational polymorphism test on one of their hereditary paraganglioma families to find out if Baysal’s hypothesis is correct.

The test, which finds mutations in small DNA fragments, normally takes a week to run, according to Willett-Brozick. She runs the test on Labor Day, 1999. “We seem to work a lot of holidays,” she says. The plans are to develop the film a week later on the following Monday. Baysal can’t wait. He goes to the lab on Saturday while Willett-Brozick attends to a previously booked weekend party at her home. Amid the Saturday afternoon revelry, her telephone rings. It’s Baysal.

“Joan! We found it!”

Richard, the principal investigator, is not convinced. The search goes on. More data. No progress. More frustration. More meetings.

At last, Richard needs no more convincing. Baysal’s comprehensive collection of data speaks volumes. There is no sign of the mutation in the region identified by the Dutch. They redirect the search.

However, more roadblocks surface. It’s now the summer of 1997, and just as Baysal is about to receive his PhD, a job offer from a pharmaceutical company lures Richard away from Pitt. Meanwhile, the ultimate results from the project are far from a sure thing. Amid all the uncertainty, Ferrell—the man most responsible for Baysal’s leaving Turkey for Pittsburgh—reassures Baysal and for good reason: “It was clear Bora was exceptional and Pitt wasn’t foolish.”

David Kupfer, chair of psychiatry, supports Baysal’s lab operations, and Bernie Devlin comes on board as the new principal investigator. (Devlin, a statistical geneticist, consults as necessary, oversees the Dutch collaboration, and makes sure the project has needed resources.) Baysal and Willett-Brozick end up discounting the region identified by the Dutch and continue systematically to weed out possible genetic contenders.

In the next two years, Baysal narrowed the search for the gene mutation to approximately 10 genes. Systematic research of those remaining genes—by Willett-Brozick’s estimate—should have taken another five years, but Baysal came up with a theory.

He had come across some obscure autopsy reports from South America written nearly 30 years ago. In those reports he noted an interesting parallel between those case studies and his families with hereditary paraganglioma.

The reports detailed how, indigenous Peruvians and Bolivians—who lived among the peaks of the Andes—frequently acquired paraganglioma. Yet, these were not instances of hereditary paraganglioma; they were isolated cases. Moreover, researchers found that the frequency of these tumors increased for inhabitants of higher elevations. Their interpretations, naturally, focused on decreased oxygen levels at higher altitudes. They noted that the most common tumor site was located along the carotid bodies.

“This is the most oxygen-sensitive tissue in the whole body,” says Baysal. “When it detects a decrease in oxygen, it stimulates the heart and lungs to work harder so the body can adapt to lower oxygen levels. If you are in a continuously low oxygen environment, like the Indians living in high altitudes, this tissue keeps working and working and working and the number of cells increases and leads, eventually, to the Indians’ tumors.

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“Joan! We found it!”

“Bora looked at the mutation not just mechanistically, not just technically; he thought, ‘What would make this tumor happen at this very point with this type of tissue?’”
What Baysal found was a mutation in the gene, named SDHD, that makes a protein eventually transported to the mitochondria—"the powerhouse and brains of the carotid bodies," according to Baysal. The mutation causes the mitochondria to react as if they were in an oxygen-deprived environment, even though that is not the case. Consequently—as experienced by Andean Mountain dwellers—this tissue never stops working. The number of cells increases, and the increased mass eventually results in tumors. Baysal also found that genomic imprinting (an unexplained male/female inheritance protocol in the genome) passed only from father to child.

"It was a moment of eureka," recalls Willett-Brozick. She marvels at how Baysal came up with his thesis:

"Bora looked at the mutation not just mechanistically, not just technically; he thought, 'What would make this tumor happen at this very point with this type of tissue?' He looked at it as a disease state, through the eyes of a medical doctor. I don't think he could have done it without his medical training. He went from a physiological approach to a biochemical approach, and then we used our genetic techniques to determine that this gene is mutant."

In February of this year, Science published the findings. (Authors included Baysal, Ferrell, Elizabeth C. Lawrence, Willett-Brozick, Devlin, Richard, five Dutch collaborators, and three MDs who provided the family materials: David Myssiorek, Wendy S. Rubinstein, and Eugene N. Myers.) The paper drew international attention, and for good reason. Though the mutation is rare, Baysal's identification of the SDHD gene's influence may well have a wide impact.

"Common cancers, not genetic in nature, have abnormalities where this gene is located," he explains. "We are postulating that these alterations may be helping those common cancer developments, through the loss of our gene, because oxygen sensing is a critical function for cells. If you remove oxygen sensing capabilities, it may help cancer cells become more aggressive."

"It will take time to put Bora's research into perspective, but I think what he discovered has the potential to be one of the more important findings to ever come out of the human genetics department," says Ferrell.

A more immediate outcome of Baysal's findings is the ability to test for the SDHD mutation. Persons with the mutation have a 90 percent chance of developing the disorder. For those who test positive, Baysal strongly suggests certain lifestyle precautions to lessen the condition's impact. If patients can avoid putting themselves into situations that make their bodies work harder to obtain enough oxygen, such as smoking or living at high altitudes, he is convinced a paraganglioma's growth could be slowed or even prevented. In addition, he recommends frequent screenings for the tumors. If they are discovered while in their infancy, they can be removed without great risk.

Ferrell points out that Baysal's findings impact not only hereditary paraganglioma and cancer research, but hypoxic conditions as well:

"Patients who are more or less similar concerning a pulmonary insufficiency or some other medical condition that leads to hypoxia will have either a relatively benign clinical course, or, if their bodies don't respond, they will have a very poor outcome. This gene may give doctors a clue as to why some patients do well and other patients don't."

For Baysal, many more late nights lie ahead. "The real issue is just now starting for aspects of oxygen sensing and whether common cancers have anything to do with SDHD or other genes involved in oxygen sensing," says Baysal. "We're trying to attack some of these questions and obtain some funding for the cancer aspect and for the genomic imprinting as well."

Baysal's six-year search may be over, but evidently his project has just begun.
The unstoppable Maud Menten never really ceased her studies. Shown here (left) at a gathering in honor of her retirement from Pitt in 1950.
Through the ice of winters and the balmy warmth of summers from 1918 to 1950, Maud Menten lurched through Shadyside and Oakland in her Model T Ford. After her jackrabbit starts, she would settle behind a wheel far taller and wider than she was, leaning slightly forward, wearing her Paris hats, blue dresses with stained-glass hues, and Buster Brown shoes. She never knew exactly which pedal to push when. Oh heavens, she would say, now, is it the middle or right one to stop and the left one to go, or middle to go, left to stop? She wasn’t sure, so she would push them all. Folks said she made up with enthusiasm and quick starts what she lacked in driving skill, and they knew to stay out of her way. On the road it was for fear of losing their lives, but elsewhere, it was because they knew she was unstoppable. Driving her Model T was about the only thing Menten couldn’t do. And if anyone tried to talk her out of anything—Arctic expeditions or mountain climbing or solving one of the most complex biochemical problems of the twentieth century—Menten, whose petite frame and sea-blue eyes projected only tenderness, would smile sweetly and keep right on doing it her way.
most subsequent enzyme-kinetic measurements. Moreover, the development of most drugs in this century would not have been possible without that understanding. When Michaelis and Menten published their work in 1913, little was known about enzymes, including their basic chemical nature.

Enzymes are protein catalysts that direct virtually all metabolic events in the body: events such as DNA and RNA synthesis, glucose production, and countless others. Enzymes speed up the rates of reactions while selectively channeling their substrates—the compounds they act on—into useful pathways to create metabolic products essential for normal bodily functioning. To make all of this possible, each enzyme has a specialized cleft on its surface, a pocket called the “active site,” that binds to its substrate to form an enzyme-substrate complex. The rate at which this binding happens determines the rate and amount of the final product. Since the development of the Michaelis-Menten Equation, this is not the guessing game it once was. The equation is taught in every undergraduate biochemistry course (though in textbooks Menten’s name is often misspelled “Menton”), and it’s used exhaustively in most research laboratories.

Beyond her work on this famous equation, Menten wrote or cowrote about 100 research papers, many of which are historic contributions. She was a primary author of a study on radiobromide and cancer that happened to be the first monograph from what was then the Rockefeller Institute for Medical Research.
If a Nobel laureate was mentioned, she was likely to ask, *What has he done since?*

(Though if you call, they’ll tell you they have never heard of her.) In addition, she uncovered the value of immunization for treating infectious diseases in animals.

More importantly, Menten is believed to be the first to study human hemoglobins using electrophoresis (an innovation widely credited to Linus Pauling, though her work on this preceded his by many years).

And with Junge and Green, she discovered the azo-dye coupling reaction. This finding is credited as the first example of enzyme histochemistry.

She wasn’t easy to please. If a Nobel laureate was mentioned, Menten was likely to ask, *What has he done since?* To a laboratory full of scientists who she thought needed to work harder, or in a new direction, she would let loose with a tirade, then fasten her hat firm as she stormed out the door, saying, *I’ve stirred them up, so now I can go.*

Menten was known for her 18-hour workdays, for delivering one-third of all daily pathology lectures as well as attending every lab session, and for being one of the most versatile scientists at Pitt.

She told colleagues that her interests revolved around pathology, oxidases, nucleic acids, tumor cells, surface tension, bacterial toxins, and pneumonia. Then there was her work with hormones, scarlet fever, and the sick youth she treated at Children’s Hospital, who loved her soft eyes and motherly expressions. And that list says nothing of her clarinet, her paintings that hung uncredited for years in the halls of Pitt, eventually finding their way into art exhibitions. Nor does it touch on her passion for astronomy or languages (she spoke at least one Native American language as well as Russian, French, German, Italian, and no one’s quite sure what else) or tea time, which she was known to observe with homemade scones and Scottish shortbread on Royal Crown Derby china.

Rain and wind lashed open coats and turned umbrellas inside out on July 11, 1979, at the University of Toronto, where, during the 11th International Congress of Biochemistry, a plaque was mounted in muddied cement with a short description of Menten’s life and accomplishments. Her portrait now hangs at Pitt, where there are memorial lectures in her honor and a named chair, but those who knew her have commented that Menten’s recognition came long past due.

Menten and Michaelis proposed this model (top), which shows that an enzymatic reaction takes place in two steps. First, the enzyme binds reversibly to its substrate, creating an enzyme-substrate (ES) complex. Second, this complex breaks down, forming the product (P) and regenerating the free enzyme (E).

The Michaelis-Menten equation illustrates that the velocity (v) of a reaction varies with the concentration of the substrate: $v = \frac{V_{\text{max}} [S]}{[S] + K_m}$. $v$ = initial velocity of the reaction, $V_{\text{max}}$ = the reaction’s maximal velocity, $K_m$ = Michaelis constant, which indicates an enzyme’s affinity for its substrate, and [S] = substrate concentration.

Armed with four degrees—including an MD and a PhD—and several published papers, Menten joined the school’s Department of Pathology in 1918 as an instructor. She retired in 1950 as full professor—a position to which she was promoted only in 1948. Then, as arthritis slowly incapacitated her, Menten, who was born in 1879 in Port Lambton, Canada, returned to her native soil, where she pursued oncolgy research at the British Columbia Medical Research Institute until her death in 1960. One of her collaborators noted, “She did not waste away. She used herself up.”

To this day, Menten is little known. The famous paper she wrote with Michaelis, in which they describe their equation for the first time, refers to her only as “Miss Menten,” according to published reports. Some called her simply “Michaelis’s assistant.” And for those who want to learn more about this mysterious woman, there is little to find. Most who knew Menten have gone, and few wrote down their thoughts and memories of her.

She was one of the first women to graduate from a Canadian medical school or practice biochemistry. She was one of the first full-time faculty members at the School of Medicine. Her work laid the groundwork for modern drug therapy and biochemistry. Yet if you ask folks about Maud Menten, about her life and her stories, you’re almost guaranteed a one-word reply: “Who?”

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**THIS TIME, E = AN ENZYME**

**THE RESULT—A NEW ERA FOR BIOCHEMISTRY**

**E + S ⇌ ES K_1**

**K_2**

**ES → E + P**

\[ V = \frac{[S] \cdot V_{\text{max}}}{[S] + K_m} \]
Using neuroimaging, Wayne Drevets is showing the world marked differences in brain structure and brain activity among those with familial mood disorders.

For example, serotonin receptors of depressed patients were only about half as prevalent, compared with controls, in the crucial region known as the midbrain raphe (Ra). The PET scan on the left captures receptor binding potential in the raphe, amygdala, and hippocampus. On the right is an MRI, which Drevets coregistered with the PET to pinpoint neuroanatomy.
hen the cable arrived, my wife and I both cried, “How can I tell you that David is gone, never to return?” The message read, in words still burned into my brain: “Sunday night he took his life.”

David was 49. He was our closest friend, a backpacking buddy, a brilliant editor and writer, magna cum laude from Harvard, creative in every way, loyal to my wife, and a pal to our son. But we also, painfully, saw David’s other side—deep, dark, despairing moods that alternated with bursts of almost boundless, unstoppable energy. We knew about the medication he swallowed in an effort at a more serene, stable life; we also knew about his close relatives who sought to end their own anguish by poison or a bullet. David chose a noose. His death was devastating, but it was scarcely a total surprise.
Serious depression, officially known as unipolar or major depressive disorder (MDD), touches more than 10 million American adults each year. Manic-depressive illness—bipolar disorder, characterized by drastic swings of mood—affects more than two million, according to National Institute of Mental Health (NIMH) estimates. Many people plunge into darkness again and again. In families like David’s, the illness runs through the generations like an ominous black thread. Counting milder forms of depression, NIMH estimates, 10 percent of the population is afflicted, and antidepressants are among the most-prescribed drugs in the physician’s armamentarium. For all their prevalence, however, the exact whys and wherefores of mood disorders have remained a tragic and recalcitrant puzzle.

At the University of Pittsburgh School of Medicine, however, Wayne C. Drevets, an MD and associate professor of psychiatry and radiology, has been fitting illuminating pieces into that puzzle. Using positron emission tomography (PET) and magnetic resonance imaging (MRI), he has demonstrated that the brains of those with familial mood disorder, both unipolar and bipolar, function abnormally during depressive episodes, and portions of their brains are actually diminished in size. One of the areas where these differences occur is a part of the forebrain known as “depression” that Drevets had identified earlier as having smaller subgenual prefrontal cortex (PFC). This region serves as a way station between what the brain’s two hemispheres, is known as the area, located behind the eyes and between the size and shape of an index finger. This is one of the areas where these differences occur is a part of the forebrain known as “depression” that Drevets had identified earlier as having smaller subgenual prefrontal cortex (PFC). This region serves as a way station between what the brain’s two hemispheres are actually diminished in size. One of the areas where these differences occur is a part of the forebrain known as “depression” that Drevets had identified earlier as having smaller subgenual prefrontal cortex (PFC). This region serves as a way station between what the brain’s two hemispheres are actually diminished in size. One of the areas where these differences occur is a part of the forebrain known as “depression” that Drevets had identified earlier as having smaller subgenual prefrontal cortex (PFC). This region serves as a way station between what the brain’s two hemispheres are actually diminish-

Overlying the two sets of images, Drevets could see that in the bipolar group the subgenual prefrontal cortex was 39 percent smaller than in the control group, and in the unipolar group it was 48 percent smaller.

A HOLY GRAIL UNEARTHED

If you want to see depression in action at the neurobiological level, you might start at the thalamus and head south a bit. Here, in the midbrain raphe, is where serotonin is synthesized. For years, scientists’ ability to measure accurately how serotonin receptors bound in the raphe of living persons was, to say the least, elusive. As Wayne Drevets puts it, this was one of clinical neuroscience’s holy grails.

However, further developing a novel radioligand (i.e., a radioisotope used to tag and measure binding activities), first applied in England, changed all that. Recently, Drevets, Ellen Frank, Chet Mathis, and others in Pitt’s Departments of Psychiatry and Radiology found that the binding potential of serotonin 1A receptors was reduced by almost half (42 percent) in the raphe of depressed persons compared with a control population. The binding potential in limbic and neocortical areas of depressed patients also was less than optimal: 25 and 33 percent lower, respectively. What’s more, those discrepancies were found among patients with both unipolar (major-depressive) and bipolar (manic-depressive) familial mood disorder—the same subgroups falling under the umbrella of illnesses known as “depression” that Drevets had identified earlier as having smaller subgenual prefrontal cortices.

—EL
Wayne Drevets with the PET scanner. He keeps handing in more evidence for neurobiological explanations of familial mood disorder.
In the subgenual prefrontal cortex, Wayne Drevets found that metabolic activity is reduced during depressive episodes. Colors show decreased glucose metabolism—the red/yellow end of the spectrum indicates the highest difference in activity relative to controls. The low activity is at least partly explained by the smaller subgenual prefrontal cortices (PFCs) in depressed persons. The bar graph compares subgenual PFC volume in Drevets’s nondepressed control group with that of bipolar (manic-depressive) and unipolar subjects during depressed episodes. The reduction is 39 percent in the bipolar and 48 percent in the unipolar.
Experts point to a subtext in the research. The fact that recurrent familial bipolar and unipolar disorder both show abnormalities in the same part of the brain indicates they are “close cousins.” Physicians should consider that relationship when choosing treatment.

ence in neuroscience, similarly praised Drevets’s research in an editorial accompanying the Nature paper. Of the PFC discrepancies reported by Drevets, he wrote, “Drevets et al. have identified a key player in one of the several systems that underlie emotional processing—a valuable finding indeed.”

For 30 years, evidence has been mounting for a neurobiological explanation of familial mood disorder. In other words, “It’s not just a matter of how your parents raised you,” to quote Goodwin, the former NIMH director and author with Kay Redfield Jamison of Manic-Depressive Illness. Indeed, the drugs that are the basis of treatment are aimed at correcting a presumed defect in the brain’s chemistry by boosting the available supply of the neurotransmitter serotonin, one of the chemicals that enable brain cells to communicate with one another.

Drevets keeps handing the neuro community more evidence. In recent research, he focused on receptors for serotonin, which allow the neurotransmitter to be taken up and reused by cells. Accurately measuring receptor action had long been a murky region of study—sort of a holy grail for clinical neuroscience. Drevets et al.’s PET scans showed marked differences in serotonin receptors for patients with familial mood disorder. Drevets also has conducted postmortem studies on brain tissue from depressed persons who died of suicide or other causes (in collaboration with Joseph Price of Washington University in St. Louis, Missouri). Sure enough, the subgenual PFCs of depressives turned out to be smaller than the subgenual PFCs of controls.

Before David J. Kupfer, chair of Pitt’s Department of Psychiatry, recruited him four years ago from Washington University, Drevets, at 39, already had earned a national reputation in neuroscience research and received a Career Development Award. Meanwhile Pitt was seeking to strengthen its acknowledged leadership in neuroscience research, especially neuroimaging.

“It was the premier psychiatry department in America,” Drevets notes in describing his decision to join Pitt’s faculty. “They saw early on that receptor imaging was going to be very important in psychiatry, and they had assembled the radiochemists and physicists to enable them to do it. Plus, it was about three times larger than Wash U.”

The workings of the human brain had intrigued Drevets since he was a junior at Wheaton College volunteering at Elgin State Hospital in Illinois.

“I developed this enduring fascination for what caused psychiatric illness,” he recalls. Drevets comes from a family of internists, and he had planned to practice cardiology. But on psychiatric rotation at the University of Kansas Medical School, he got his first glimpse of the potential of brain imaging.

“I quickly saw it as a way to understand the pathophysiology of psychiatric disorder,” he says.

At “Wash U,” he was mentored by Marcus Raichle, whom he recognizes as “one of the true pioneers of imaging.” Drevets spent 10 years in St. Louis, then moved to Pitt’s School of Medicine.

Since then, Drevets has done his part to stir up conventional wisdom. His postmortem studies revealed a striking finding: The depressed brain had lost glial cells, yet the functioning neuron count was normal. That was big news. Glia have long been considered scaffolding that supports functioning neurons, yet they appear to do much more than science had recognized. Researchers have found that among other responsibilities, these numerous cells store glucose and play a role in neuronal metabolism. Some types equipped with serotonin receptors help to innervate the brain with that important neurotransmitter. If the brain loses glia, less serotonin might be available, and thus the brain might not be as well equipped to fight itself from attacks of depression.

The link between loss of glia and depression isn’t clear, Drevets says, “but what we know is that in depression, there are too few glia.”

All this raises one of those chicken-or-egg questions: Does an episode of depression trigger changes in the brain, such as lower glia counts and subgenual PFC volumes; or is depression brought on by existing brain abnormalities? Or rather, is “malignant sadness” caused by an interaction between the two? Drevets is now aggressively seeking those answers, studying the same patients when they are depressed and when they have emerged from depression. Preliminary results seem to indicate that some abnormalities are persistent and may serve as markers for the illness. He also has begun to perform PET and MRI imaging on “high risk” young adults (meaning people who have more than one family member affected) to see whether abnormalities might predate the first episodes of depression.

Other questions arise, too. Do repeated episodes of depression cause damage in other parts of the body, the way hypertension or diabetes assaults the blood vessels, the heart, and the kidneys? Is there a way to target drugs directly to the deficient areas where they are needed? Finally, is there some distinct anatomical or neurochemical marker detectable with a brain image by which those vulnerable to depression could be picked out in advance?

The benefits of Drevets’s research to diagnosis and treatment of mood disorders will be played out largely in the future. Yet Goodwin, who is now director of the psychopharmacology research center at George Washington University, points to a subtext in the research of potential importance to treatment now. The fact that recurrent familial bipolar and unipolar disorders both show abnormalities in the same part of the brain indicates they are “close cousins.” Physicians should consider that relationship when choosing treatment. They should also note, Goodwin cautions, that both conditions are different from what happens when a man suffers from a single bout of depression after losing his job.

“Our work in imaging has led us to clues we knew nothing about beforehand,” Drevets says.

“We don’t yet know what sets what in motion. We now know the important things to study. The kind of information we’re getting may well account for why treatments work. [It] may also lead to an understanding of how we should be treating people more effectively in the future.”

Let’s hope that understanding will save the lives of future Davids.
Anh Lam, MD ’03, stands on the 10th floor of the Biomedical Science Tower, staring apprehensively at a floor-to-ceiling black cylinder, just large enough to hold a person.

“That’s the scary black revolving door,” she jokes. “I’m always afraid I’m going to get stuck.” With a deep breath, Lam, who just finished her first year as a University of Pittsburgh medical student, steps inside the tube, grabs a handle, and rotates the walls around her until she is in a nearly pitch-black room. As her eyes adjust to the darkness, a red halo of light directs her toward the film developer in the corner. It groans as Lam inserts an undeveloped film of gel electrophoresis. She has worked in a few labs (has even conducted her own projects at the National Institutes of Health), but this is the first time she has done this particular technique, called the electrophoretic mobility shift assay (EMSA), so she is eager for the results. Yet, with arms folded, she can only wait.
FROM LEFT: Susan Manzi, Chris Thunberg, and Joseph Ahearn spent their summer talking a lot about lupus. Manzi is an MD/MPH and, though not formally part of the summer research program, volunteered to take Thunberg into the clinic to see lupus from that perspective to complement Ahearn’s work with him in the lab.
“Asking the unanswerable question may be good cocktail party conversation. However, in terms of the day-to-day life in the laboratory or in the clinic, asking the answerable question is key.”

Lam is one of about 30 medical students who spent their summer vacations in research laboratories through the Medical Student Summer Research Program at Pitt. The program, which has been around since the ‘60s, lets physicians-in-training experience the research side of medicine, working closely with a faculty mentor. With the forecast for the next generation of physician-scientists looking meager in terms of numbers, the program hopes to inspire some students to pursue research careers, but by no means is that the program’s only goal.

“Research experience is just as important for students who will go into private practice,” says Stephen Phillips, associate dean of graduate studies and director of the program. “As physicians, they’re the beneficiaries of discovery. They prescribe drugs or procedures whose origins are in scientific research, and they need to find out from personal experience what discovery is all about.” So for eight weeks, students pair up with faculty mentors to collaborate on a research project.

Anh Lam got a good dose of discovery this summer. In addition to working on two research projects, she watched her first surgery, and found herself in exam rooms observing doctor-patient interactions. On top of all this, Lam got to work alongside Jennifer Rubin Grandis, associate professor of otolaryngology and pharmacology.

Grandis thinks part of her job as a mentor is not only to guide students in conducting research and foster their excitement for science but to show them they shouldn’t underestimate what they can accomplish, professionally and personally.

“My hope,” says Grandis, “is that some of these students will get turned on enough that someday they’ll think, Oh yeah, I can do [that]. She had a family, saw her kids, wrote grants and papers, took care of her patients, and even baked muffins.”

Grandis (MD ’87) was a mentee in earlier years of Pitt’s research program—and she doesn’t mince words in describing her experience: It was horrible. She spent the summer avoiding what she calls “the French Revolution thing.” Alone in a laboratory with cages and cages of rats, Grandis was charged with decapitating them for endocrine studies. “The only thing I remember about that summer,” she jokes, “is that I bribed a technician. I paid her my entire stipend to kill those rats for me. It didn’t inspire me to go into science.”

Phillips remembers Grandis’s experience well, and he shakes his head as he tells the story. “Not everyone can be a good mentor for this kind of project: a compressed, very well defined, summer of intensive direction.” But Phillips has learned a lot in his 30 years of involvement with the program. He has a network of colleagues that he depends on for pairing students with the right mentors.

“That first experience is the most crucial in the life of a serious student who wants to explore whether research is for them,” he says. “You can wreck them for life if you don’t do it right.” Fortunately, Grandis went on to find other mentors, and now her life revolves around science. But her first experience took a toll, and she wants to make sure that doesn’t happen to her students. So each mentee who comes through her lab is given a project to investigate alongside others—usually residents, postdocs, undergraduates, and several technicians. Grandis makes sure Lam and other program participants do original research.

Lam spent part of her summer working on a phase-one gene therapy trial for treating squamous cell carcinomas of the head and neck. She spent countless hours extracting DNA from animal tissues and checking for localization of the therapeutic gene to determine whether it stayed in the area where it was injected. The rest of her time, Lam worked on the EMSAs she developed in the darkroom behind the black revolving door. These gels will be used as a tool for determining the activity of proteins that regulate genes that may be important in cancer development. With these EMSAs, Grandis’s lab hopes to develop methods for blocking the activation of cancer-causing genes.
Before Lam braved the black revolving door, she jerked open a freezer kept at -80 degrees Celsius and pulled out a film cartridge about the size of a notepad. “This is the first time I’ve done this particular technique,” she said, brushing ice crystals from the plastic and rotating the cartridge in the air, as though it offered clues about the gel inside.

It’s an everyday occurrence in labs everywhere, but it’s also a moment of bated breath and expectation. The results of this EMSA will help Lam decide where to take her project from here. With each answer unveiled, a researcher, such as Lam, advances her knowledge an increment forward, opening up new questions that can keep her going in the same direction, or pointing toward completely new paths.

The same is true for good clinicians doing diagnostic work.

“Research is about asking questions of the unknown,” says Phillips, “and designing experimental systems that will provide answers.

“Sometimes these things can be traced back 20 or more years to show that no one has done an experiment in decades to revise what has been said.”

“The art of differential diagnosis involves knowing the questions to ask that enable you to arrive at the likely cause of disease.” In the laboratory and the clinic, successful investigators don’t just ask questions—they ask answerable questions.

“Sometimes these things can be traced back 20 or more years to show that no one has done an experiment in decades to revise what has been said.”

Don’t blindly accept anything as truth, he tells students, without first seeking evidence that supports it.

Sometimes these things can be traced back 20 or more years to show that no one has done an experiment in decades to revise what has been said,” he explains. “So being a good investigator isn’t just about asking questions, but questioning what supposedly is truth and realizing that maybe there’s another explanation.”

That’s hitting home for Chris Thunberg, MD ’03, who’s working with Ahearn this summer. Three floors down from the room where Lam stands blanketed in darkness waiting for her gel, Thunberg stands at his meticulously organized lab bench. The soft sound of clinking glass is muffled by the hum of industrial freezers as Thunberg washes tissue samples he hopes will shed light on the autoimmune inflammatory connective tissue disease known as systemic lupus erythematosus.

Thunberg’s project funding is the result of a national competition sponsored by the American College of Rheumatology. That funding has enabled him to augment his summer experience by working with Susan Manzi, an MD/MPH, this fall. In that phase of the project, he’ll gain experience with lupus from a clinical perspective.

He is getting a good feel for what makes for a successful career as a physician scientist.

“Working with Dr. Ahearn,” says Thunberg, “it’s clear that one requirement is thinking outside the box.”

“Check it out,” says Dyer, “this is a band that’s higher than the ones we’ve seen.”

“Does that mean it bound better?” wonders Lam.

“It means different,” he replies.

Two lean in and go over every detail on the film. One result isn’t what either of them expected.

“I don’t know what to make of this one,” says Dyer. “It’s a trip.”

They talk about new directions for the experiment that might shed light on this surprising result. Lam is eager to pursue the finding. She talks passionately about further studies. And she thinks about her mentor, then rushes to the black revolving door.

“Do you know where Jen is?” she asks, full of excitement.

“I want to show her this. I know she’ll want to see it.”
coursecwork is tailored for
junior faculty and trainees
in the health sciences.

Limbach is a successful
entrepreneur himself. So
when he heard about the
need to expose physicians
and researchers to business
concepts to foster biotechnology
products and spin-offs, it caught his attention.
He sees the center one day
supporting health sciences
work throughout the
University, as part of an
effort to spawn biotech economic development
in western Pennsylvania.

A few strategic investments could yield
handsome payoffs in advancing medical
research, Limbach and other center organizers
believe. They especially want to encourage
talented young investigators who find it tough to
get grants. (When their research is in the initial
stages, it might be overlooked by agencies such as
the National Institutes of Health.) The cen-
ter plans to offer “preseed” funds for promising
projects, to come from gifts such as Limbach’s.
After all, there are bound to be a few scientific
blue chips in there somewhere.

DOGGED DOCTORING

O’LEARY’S SPIRITED EXAMPLE

BY MARK JACOBS

The turkey is carved, the stuffing scooped
and waiting in a dish, but the phone
rings, and Eugene F. O’Leary, MD ’51,
has to leave the Thanksgiving table to attend
to yet another flu patient: There is an out-
break of influenza in western Pennsylvania.
His daughter Linda O’Leary remembers hav-
ing to eat her turkey by the telephone because
it rang so often that day.

The son of a steelworker who lost his leg in
a railroad accident, O’Leary grew up in Belle
Vernon, Pennsylvania. (He would one day
return to set up a general practice there and
in nearby Monessen.) In 1943, he enrolled at Pitt
but joined the army after his freshman year.
He found himself on the Siegfried Line, where
German shrapnel ripped into his leg, requiring
him to spend several months recovering in
England before returning home and to Pitt.
There he focused on finishing his undergrad-
uate work and enrolling in the medical school.

O’Leary planned to specialize in cardiology—in fact, he interned with Michael
DeBakey and Denton Cooley in Houston.
Once he began his practice though, he found
that the demands of family medicine absorbed
his attention. He was known as a first-rate
diagnostician and also delivered some 3,000
babies during the course of his career.

The doctor had a sly side as well, yet his
designs were always for a worthy cause.

O’Leary would give a slight slap on a
wrist to distract a fearful child from the
needle he placed in the other arm. And for
opening day of the 1954 baseball season, he
and a friend flew the milk run to St. Louis
to see his hero, hitting-sensation Stan
Musial. They left late Monday night and
arrived in the bleary early hours of Tuesday.
A tall tale woven around
O’Leary being called to St.
Louis to perform an
important operation got
them a room in a town of
booked hotels. Then,
somehow, they managed to
spend Tuesday evening
chumming with “The
Man” himself. (O’Leary,
obviously a spirited fan,
thought nothing of flying
back for just about every
Panther football game dur-
ing the several years he lived
in La Jolla, California.)

Eugene O’Leary died in 1998; in his honor,
his wife, Mary Lou O’Leary, recently estab-
lished two endowments at the medical school
in his name. One fund will be used for much-
needed scholarships, the other for student
recruitment and retention efforts.

O’Leary’s memory persists in many ways
besides those generous gifts. Not too long
ago, Chaney Rockwell, the doctor’s four-
year-old great-grandson, quizzed Mary Lou
O’Leary on the difference between a com-
pound and a mixture. When she asked
whether he knew, he smiled slightly and
said, with signature O’Leary determination,
“Yes, but you tell me first.”

GOING PUBLIC

ENTREPRENEURIAL MEDICINE

BY ERICA LLOYD

let’s run down that list of courses for the
aspiring cellular biologist one more
time: There’s Membrane Trafficking,
Integrative Physiology, and, oh, at some point
along the way, make sure you take Competing
in a Global Environment.

The rate of biomedical discovery today is so
rapid, researchers might try to read a journal a
day attempting to keep up. Officials at the
University of Pittsburgh Cancer Institute (UPCI)
are hoping that Pitt scientists will add a few less
conventional subjects to their continuing edu-
cation endeavors—and become versed in areas
like teamwork and strategic management.

This year, a donation from businessman
Scott Limbach made it possible for UPCI to
establish a center to promote medical entrepre-
neurialism at Pitt. The Scott Limbach Center
for Medical Entrepreneurship is particularly
focused on helping investigators move their
innovations—novel therapies or diagnostic
techniques, for example—from the lab to the
marketplace. A program in the business school
is one of the first to come out of the center. Its
Crunched in the fetal position, an elderly woman arrives at a Cambridge, Massachusetts hospital after months, perhaps years, of neglect. Nobody knows her name. She is silent, except for an occasional groan that most likely stems from the pain of an infected and ulcerated bedsore covering her entire lower back.

The hospital staff admits her immediately. So that she can undergo treatment for the bedsore, dehydration, and other serious ailments, a 23-year-old orderly is charged with lifting this frail, knotted woman out of bed and positioning her in a way that the nurses and physicians can attend to her.

Moving gravely ill, incommunicative people is not something the orderly prepared for in his humanities classes. That’s because most honors graduates from the University of Chicago don’t aspire to be orderlies. David Barnard was no exception. Upon graduation in 1970, he was awarded a fellowship in history at Brandeis University. But Vietnam changed those plans. It was time for Barnard to fight for his country or fight for his ideals. He declared himself a conscientious objector.

This required him to perform alternative service. He remembers what the draft board told him: “You should not make much money, you should suffer a little bit, and you should do something humanitarian.” The board suggested “the hospital route.”
His first encounter with the elderly, bedridden woman would be like many others.

Hi, I'm David.

No response.

I need to move you so the nurses can tend to you.

Barnard shifts her position—delicately—cringing inside at the thought of adding to her pain. He gets her settled.

Still no eye contact. He fluffs a pillow, adjusts the blinds. There must be more he can do.

It's bright and sunny today. See? Maybe that will help you feel better.

Nothing.

I'll be back in a bit to see how you're doing.

Barnard's monologue continues for weeks. One day, he tries again to position her comfortably. As he is about to leave, he thinks he hears something—a mumble? He stoops down close to the woman with the blank stare, lowering his ear beside her mouth and hears these words:

“Thank you.”

Eventually, he said more. She was speaking softly and with difficulty, but she was speaking.

Barnard learned her name. (We'll call her Sarah Hale.) He also learned she was good company.

Before long, Hale was telling Barnard stories about her life. She had never married. And she liked to reminisce about her high-flying days as a student at Wellesley College at the beginning of the 20th century.

One time, they were going through their repositioning routine, and just as he was about to move her, Barnard said, “This might sting a bit. Grit your teeth.”

“I don’t have any teeth,” she quipped back.

“All right then, grit your gums.”

Hale’s condition improved to the point where she was ready to be released. Her new friends, Barnard and the other orderlies, hosted a going-away tea party on her behalf. That afternoon, the tears flowed as freely as the tea.

Once his alternative service was completed, Barnard was permitted to resume his history studies. Instead, he resigned from the Brandeis fellowship. Health care was the field for him, though he didn’t see himself as a clinician:

“I realized, through the experiences I had, that beyond the technology . . . there is something very powerful that can happen at a human level. I wanted to learn more about that. I felt maybe there was a way I could contribute to training other people in medicine how to function while keeping that dimension in view.”

Today, Barnard is a PhD in medical humanities and professor of medicine at the University of Pittsburgh School of Medicine, where he teaches ethics courses. He also directs the palliative care education program in the University’s Center for Bioethics and Health Law. This year, Oxford University Press came out with his new book (he’s one of four coauthors), Crossing Over: Narratives of Palliative Care.

The Oxford Textbook of Palliative Medicine devotes more than 1,300 pages to the subject. Barnard praises that publication, yet he notes, “Life is much more complicated than a textbook.” In order to give the medical community a flesh and blood perspective in areas ranging from pain management to spiritual concerns, Crossing Over presents patients with terminal illness not as case studies, but as people. Its authors capture the voices of patients, family members, and caregivers in the midst of struggle:

“If I could pull God down from heaven, I’d beat him up.”

“She’s not going to die from an overdose of ice cream.”

These are voices Barnard wants heard. They’re voices he started listening to nearly three decades ago when Sarah Hale whispered, “Thank you.”

Eventually, she said more. She was speaking softly and with difficulty, but she was speaking.
Regan was born on St. Patrick’s Day, so she got to wear a green hat. Her mother, Dawn Lynn Check, remembers how quickly nurses replaced the hat with an intravenous line, feeding it into a thread-like vein on her shaved scalp. Regan, now a stubborn yet sociable 19-month-old, fought back when doctors ran a central line to her heart and inserted tubes to bolster her tiny lungs as one deflated, then the other.

That feistiness was a good sign, medical staff told Check, who had given birth to her third child six weeks early. Check remembers how—as they confidently tended to her daughter’s physical needs—the doctors and nurses taught her, the parent, how to love her seemingly fragile new child. Don’t just brush a hand over her, they urged. Don’t caress her lightly. Lay a firm hand on her. Be strong for her.

Check says Regan absorbed that strength. The toddler with blonde pigtails loves to be hugged and held but also fearlessly explores her outdoor surroundings in the company of the family dog, George. When no one is watching, the dog-child duo raids the kitchen cabinets for cookies and steals Matchbox cars from Regan’s older brothers to throw down the laundry chute.

Last year, Check, who is a minister and executive director of United Campus Ministry of Pittsburgh, was invited to speak at the School of Medicine-sponsored memorial service that honors those who donated their bodies to advance medical science. Busy caring for Regan, she didn’t make it.

This year, on a warm May afternoon in Heinz Chapel, Check takes the pulpit at the Humanity Gifts Registry Memorial Service to tell medical students and family members of donors that, in a sense, Regan is alive because of those noble contributions. Just as she will never forget the compassion and medical skill that saved her daughter’s life, Check hopes medical students never forget the lives that enrich their education.

Today, students publicly remember. No dulcet organ accompaniments or sprays of flowers are necessary. L. Mark Lockett, a member of the Class of 2003, shares a eulogy he wrote with his classmates. They were craftspersons and tradespeople, professionals, and homemakers; some lived well into their nineties, while others may have died early, untimely deaths. . . . Three other students take turns reading the names of 73 Pennsylvanians who donated their bodies for medical education in the past year. The names are uttered with reverence, careful not to mispronounce. Seventy-three more lives.

Seventy-three more stories, some of which may also begin with tales of Matchbox cars, cookie raids, and firm yet tender caresses.

Each name is read; soon, it’s time again to step outside the chapel, where lawnmowers rumble, robins set up house, and tulips etch their brief tall moments scarlet against the sky. It is the kind of day that makes you think of life cycles. The words of a minister echo: “What I hope the medical community will learn is not just how to do a job, but about the gift of real life.

“Life bound up by love.”
CLASS NOTES

'40s  ROY CHARLES MONSOUR, MD ’43, still practices full-time at the age of 83. He practices in Jeannette, Pennsylvania, and was just named a fellow of the American Academy of Family Physicians.

'50s  CYRIL H. WECHT, MD ’56, of Pittsburgh, was one of the recipients of the first Annual Community Recognition Awards, given by the William P. Fralic Foundation. (Bill Fralic was a Pitt All-American and Atlanta Falcon All-Pro.)

'80s  KEVIN O’TTOLE, MD ’83, is an associate professor in the Department of Emergency Medicine as well as associate director of emergency medicine and director of hyperbaric medicine at UPMC Presbyterian.

'90s  KEVIN P. HAYES, MD ’90, is associate medical director and vice-president of UnumProvident Insurance in Los Angeles, California. He serves as clinical instructor of psychiatry at the UCLA School of Medicine.

DIANA L. (BUSHELSS) METZGER, MD ’91, was assistant professor of clinical medicine at Ohio State University before moving to Orange Park, Florida, to join Clay Cardiology.

EMANUEL N. VERGIS, MD ’91, is now associate clinical chief in the Division of Infectious Diseases at UPMC Health System after receiving an MPH in epidemiology from Pitt’s Graduate School of Public Health in 1999. He can be reached at verge@pitt.edu.

JODI SEGAL, MD ’94, received a master’s in public health in 1998 from Johns Hopkins University, in Baltimore, Maryland. She joined the faculty there in July as a general internist, with an appointment to conduct clinical research in the Division of Hematology.

AMY HURRIANKO WEBER, MD ’96, has completed her residency in ophthalmology at Wills Eye Hospital, in Philadelphia, Pennsylvania, and was given the Ketan Patel Award for her professionalism, compassion, and care for patients. She can be contacted at aaweber@earthlink.net.

LYNN E. TAYLOR and CHRISTINE HENDRICKSON, both MD ’97, were recognized as the best resident teachers by the senior class at Brown University’s medical school. Taylor writes that she is an attending physician at the Miriam Hospital’s Immunology Center, also in Providence, Rhode Island, caring for HIV-positive patients and those who are HIV-negative but considered at high risk for contracting the virus. —MJ

REUNIONS

The CLASS OF ‘55 is one that Medical Alumni Association (MAA) officials would like to “clone for its enthusiasm.” This year’s July 16-19 reunion did nothing to alter that opinion. Held at Seven Springs Mountain Resort in the rolling hills of western Pennsylvania, the four-day retreat included great food, local sightseeing tours, ongoing games of bridge, and, of course, lots of great golf. (Although none shot their age.) Among the speakers at the surf-and-turf dinner finale was Samuel A. Tisherman, MD ’85, whose late father, Samuel E. Tisherman, MD ’55, had been the doctors’ classmate. The younger Tisherman’s ties to Pitt also run deep: He is married to Susan Dunmire, MAA president, and teaches surgery and anesthesiology/critical medicine at UPMC Presbyterian.

The Owl, 1983

ALUMNI NEWS

SUSAN M. DUNMIRE, MD ’85, President
ROBERT BRAGDON, MD ’73, President-elect
PAUL M. PARIS, MD ’76, Vice-president
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PETER SHEPTAK, MD ’63, Member-at-large
JOANN NARDUZZI, MD ’62, Member-at-large
JENNIFER RUBIN GRANDIS, MD ’87, Member-at-large
ROSS MUSGRAVE, MD ’43, Executive Director
M-245 Scaife Hall
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Pittsburgh, PA 15261
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medalum@medschool.pitt.edu

The Owl, 1945

ILLUSTRATION: BECKY SMITH

M EDI C A L A LU M NI A SSOCIA T I ON OFFICERS
For Kenneth D. Rogers, a doctor’s job didn’t start after a patient became ill. It began on a street corner where a 13-year-old boy was about to smoke a cigarette for the first time.

“Ken was involved in public health long before it was fashionable to do so,” recalls Seymour Grufferman, a professor of family medicine at the University of Pittsburgh School of Medicine. “In many ways, he was ahead of his time.”

Rogers’s time at the School of Medicine began in 1953, after earning his MD at the University of Cincinnati and serving as a navy surgeon in World War II. By 1960, he was chair of the Department of Community Medicine. He held that position and also was a professor of pediatrics until 1988, when Grufferman succeeded him as the department chair. During his tenure, Rogers established a slew of community programs that had one common denominator: keeping people well. Rogers helped found the Matilda Theiss Health Center and was active in the Western Pennsylvania Health Preceptorship Program, to name just a few of the ways he directed his passion for community work. He died this June at the age of 79, and his contributions are more than remembered.

“Right now we’re embarking on a prophylactic pneumococcal vaccination program with all of our 17 University affiliated hospitals,” says Donald Middleton, interim chair of the family medicine department (the grandchild of community medicine). Many such preventive medicine programs in Pittsburgh exist in large part because Rogers and others like him planted those seeds at the University, notes Middleton. He adds that the preventive health community will deeply miss Rogers’s insight and critical skills.

—RM

IN MEMORIAM

ROBERT C. BURT (MD ’41) JUNE 5, 2000
JOHN J. CONLEY (MD ’37) SEPTEMBER 21, 1999
JULIUS A. FINO (MD ’43) MAY 30, 2000
JAMES R. HUGHEY (MD ’44) JUNE 22, 2000
WILLIAM C. JONES (MD ’53) APRIL 24, 2000
PAUL L. KLOSE (MD ’52) APRIL 30, 2000
GEORGE W. PATTERSON (MD ’36) MAY 19, 2000
KENNETH D. ROGERS (FACULTY) JUNE 6, 2000
MILTON SINGER (MD ’43) JULY 20, 1999
It was during her residency, on an emergency flight—a tractor trailer had plummeted off a bridge, onto the road below, and landed on a car—when Susan Dunmire, MD '85, knew the medical life was for her. “We landed the helicopter,” says Dunmire, “and saw the crushed car. The trailer had killed everyone in the family but a 10-year-old girl. But despite all she’d been through, she knew what had happened, and on the way to the hospital, she said to me, ‘I have no one else in the world now; please stay with me.’ I did. I held her hand, and I stayed with her. And I knew then, this was what I wanted to do.”

Though medicine was part of her daily learning, until that awful day, it never rang true. Yet it was in her blood. As a child, Dunmire would go on Saturday morning rounds with her father, Lester A. Dunmire, MD '48. She recalls those quiet moments, watching her dad with patients, as he held hands and listened to stories.

Today, when she’s with students, when she sees patients, Dunmire remembers his words. No matter how tired you are, when you see patients, sit down with them, hold their hand, and give them all the time it takes to answer their questions and get through their fears.

A tradition of compassion runs deep in her family. Dunmire’s maternal grandfather, Harold Mitchell, MD ’21, was once chair of the Department of Neurology at Pitt. “Up until the day he retired, my grandfather made house calls in poverty-stricken areas—places no one else would go,” says Dunmire. Mitchell came from poor rural roots himself, riding a horse into Pittsburgh to attend medical school. At the heart of his philosophy for doctoring, for life, was a simple belief: No one was better than anyone else.

Dunmire is an emergency department (ED) physician at UPMC Presbyterian; and like her father and grandfather before she is a teacher. As an associate professor of emergency medicine, she conducts a fourth-year elective in emergency medicine. She also is on a physician team that presents case studies to second-year students in preparation for their boards. In addition, she has created an interactive computer course to augment students’ ED experiences.

“Once,” she explains, “we just taught whatever came into the ED. Now, students can be introduced to cases outside the ED, on the computer, and discuss them. It’s a constructive way to continue learning.” This year, students recognized Dunmire’s dedication by giving her the school’s Golden Apple award for teaching.

The Medical Alumni Association (MAA) is now a direct beneficiary of Dunmire’s fidelity and talents. She will serve this year as the association’s president, and she is ready to dig in.

“I’m going to sit at that table with alumni—some of them my teachers, my mentors—and learn,” she says. She also wants to use her position, as someone who works closely with students as a professor and advisor, to serve as a bridge.

“I’m going to offer ways to relate to students, address issues relevant to them, and with the MAA, learn how to best serve them.”

One need the MAA has already identified, and Dunmire wholeheartedly embraces, is building on the number of student scholarships it offers. That way, new graduates can focus more on patient care and not be distracted by their debt load.

Even higher up on Dunmire’s wish list is increasing the number of alumni involved in the med school. “Get them involved with the students as teachers, as mentors, as role models,” she says. Little wonder. Dunmire, after all, is living testimony to the value of passing knowledge and experience from one generation of physicians and teachers to another.
These dapper young men were found in the 1956 Hippocratean. Fill us in on the who, what, where, and, especially, why and win a lifetime subscription to Pitt Med and, depending on availability, a Kewpie doll or a case of Turtle Wax. Also, if you have a Pitt Med moment to share, send it our way.
CALENDAR

OCTOBER 5
MARSHALL S. LEVY, MD
MEMORIAL LECTURE
Henry J. Mankin, MD ’53, Speaker
“Osteoarthritis and the Healing of Cartilage”
Reception, 5 p.m. Lecture, 6 p.m.
West Wing Auditorium, UPMC Shadyside

OCTOBER 26
2000 PETER AND EVA SAFAR LECTURE FOR THE SCIENCES AND HUMANITIES
John B. Anderson, Speaker
“On the Pathogenesis and Prevention of Mass Killings”
Lecture Rooms 5 and 6
Scaife Hall, 4 p.m.

OCTOBER 27
LEGACY LAUREATE LECTURE
Bernard Fisher, MD ’43, Speaker
“Insularity with Vision, a Paradigm for Scientific Productivity: 914 Scaife Hall”
Lecture Rooms 5 and 6
Scaife Hall, 8 a.m.

OCTOBER 30
ALUMNI AND FRIENDS RECEPTION
New Orleans Room
Hyatt Regency, Chicago, 6 - 7:30 p.m.
For information
Ross H. Musgrave, MD ’43
412-648-9090
medalum@medschool.pitt.edu

NOVEMBER 4
CLASS OF ’75 REUNION
Top of the Triangle
Pittsburgh, PA
For information
Barbara Zawadzki, MD ’75
412-361-2343

NOVEMBER 10 AND 11
MUSGRAVE LECTURESHP
November 10, 5 p.m.
Robert M. Goldwyn, MD, Speaker
Magee-Womens Hospital Auditorium
November 11, 10 a.m.
Surgery Grand Rounds
Lecture Room 6, Scaife Hall
For information
Ross H. Musgrave, MD ’43
412-648-9090
medalum@medschool.pitt.edu

MAY 18
SENIOR CLASS LUNCHEON
Twentieth Century Club
and
ANNUAL ALUMNI DINNER DANCE
Pittsburgh Athletic Association
Pittsburgh, PA
For information
Ross H. Musgrave, MD ’43
412-648-9090
medalum@medschool.pitt.edu

MAY 18 AND 19
CLASS OF ’91 REUNION
Pittsburgh, PA
For information
Andy Miller, MD ’91
508-650-9181
andymiller66@hotmail.com

MAY 19
DEAN’S BREAKFAST MEETING
Scaife Hall
For information
Ross H. Musgrave, MD ’43
412-648-9090
medalum@medschool.pitt.edu

SO THAT ALUMNI AND FRIENDS CAN GET A FEEL FOR THE MANY ACTIVITIES THE SCHOOL SPONSORS, WE’VE INCLUDED INFORMATION ON FALL EVENTS THAT HAVE TAKEN PLACE AS WELL AS THOSE YOU MAY WANT TO ADD TO YOUR CALENDAR.
TO FIND OUT WHAT ELSE IS HAPPENING AT THE MEDICAL SCHOOL... http://www.health.pitt.edu
SPECIAL DELIVERY

Neither rain, nor snow, nor sleet, nor hail should prevent you from contacting your long-lost classmates. That’s because the new University of Pittsburgh School of Medicine alumni directory has been released this month and those of you who ordered a copy will receive it soon. If you haven’t placed an order, you can still reserve one by contacting our directory publisher:

Customer Service Department
Bernard C. Harris Publishing Co.
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You won’t be disappointed. This comprehensive reference source is a compilation of the most current data available on the school’s alumni. There are thousands of listings, which probably include more than a few of your old friends. So, no more excuses for not staying in touch.