

PITTMED

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CONTRIBUTORS

MICHAEL ROSENWALD—["Nurse, Wrench Please"] Michael Rosenwald is a full-time staff writer for *In Pittsburgh Weekly*. In his spare time he freelances for a number of organizations, including *The New York Times*, *The Boston Globe*, and *Associated Press*, and worries about his health. Rosenwald is a self-proclaimed hypochondriac who considers writing for *Pitt Med* his dream job. He currently is recovering from mononucleosis, a condition that was actually confirmed by a licensed physician.

PAM FRANCIS—[Cover and "The Switch"] Pam Francis is an editorial and advertising portrait photographer whose work and personal life keep her on the road. She recently returned from a month of travel—first stop, a photo shoot in Slovakia for an annual report, then she was off to the British Virgin Islands. But that was just for fun. Her work has appeared in *Time*, *Newsweek*, *Fortune*, *Texas Monthly*, and *People Weekly*.

COVER

Bert O'Malley, MD '63, keeps his colleagues on their toes. (Photo by Pam Francis)



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Do his postdocs get microscopes or whoopee cushions? Bert O'Malley, MD '63, landmark hormone researcher and creator of the GeneSwitch, just won't take himself seriously. He says science is serious enough.

BY REBECCA SKLOOT

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For decades, Philip Hench, MD '20, would not give up his belief that our bodies produce a mysterious antirheumatic. He shared the Nobel for his discovery of cortisone; yet science still struggles with his larger goal, offering respite to sufferers of rheumatoid arthritis.

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Massimo Trucco: He may be just a few nucleotides away from a vaccine for juvenile diabetes.

BY ERICA LLOYD

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The University of Pittsburgh is an affirmative action, equal opportunity institution.

Philip Hench (MD '20) spent decades chasing what most of his colleagues thought was a ghost. He believed our bodies were capable of producing a mysterious substance that could offer respite to sufferers of rheumatoid arthritis. In the end, Hench triumphed over his naysayers. He did not find a cure for rheumatoid arthritis; but he did unveil the extraordinary power of a steroid he named "cortisone," a therapeutic from which millions still benefit today. (I encourage you to read Rebecca Skloot's feature, which begins on page 12.)

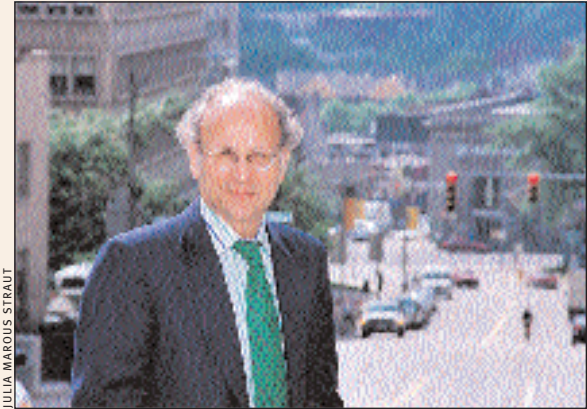
Dr. Hench was a classic physician-scientist. As both a clinician and a basic researcher, he was able to quickly move medical research findings from the bench to the bedside. And his legendary passion for his work must have been shaped by the patients he saw regularly—people for whom recurring pain and disability were part of the fabric of daily living.

Though they may admire the Philip Henches of the world, our young MDs are not choosing careers that include basic or clinical research. They typically are faced with staggering debts on graduation and feel they cannot afford to pursue apprenticeships as scientists in addition to clinical training.

The physician-scientist is "endangered and essential," to cite Princeton University's Leon Rosenberg (*Science*, January 1999). The number of first-time MD applicants for NIH research project grants has plummeted in the past few years. At the current rate, there will be no first-time MD applicants in 2003. As these statistics play out, they have the potential to undo the scaffold of medical science and this country's primacy as the fount of medical research. Physician-scientists ask important research questions inspired by patient conditions; they offer priceless perspective to collaborators in the basic sciences and in clinical settings; and they can make the strongest case for the clinical relevance of basic research to legislators and agencies. They play a vital role in advancing medical science.

The University of Pittsburgh School of Medicine is creating an environment that nurtures and encourages physician inquiry. Through a new physician-scientist training program, we hope to entice young MDs who have the creativity and talent to build outstanding academic careers to pursue more rigorous scientific training.

Our hope is that this new generation of physician-scientists will follow Dr. Hench's lead, and not shy away from chasing down a few ghosts along the way.



JULIA MAROUS STRAUT

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



Devoted to noteworthy happenings at the medical school. . . Also, to stay abreast of Pitt health sciences news, including info on faculty and research, see <http://www.health-sciences.pitt.edu>

Faculty Snapshots

A SAMPLING OF SOME OF THE PITT SCHOOL OF MEDICINE FACULTY'S EXCITING WORK:

Ellen Frank, professor of psychiatry and psychology, reported that disruptions to daily routines, or social rhythms, increase the risk of mania in patients with bipolar disorder. In her recent study, Frank illustrated that drug therapy combined with interpersonal and social rhythm therapy—a technique that focuses on regulating daily routines and improving interpersonal relations—was most effective for long-term remission of bipolar disorder. The disorder affects at least two million Americans. Traditional treatments, such as lithium, work well short-term, but none have had clear long-term success.



Frank

A team led by **Michael J. Fine**, associate professor of medicine, has been awarded a major grant from the Agency for Health Care Policy and Research for its work with community-acquired pneumonia (CAP). CAP is the fifth-leading cause of death in the United States with an annual cost, due to morbidity, of \$9.7 billion. Fine's research project is aimed at reducing the number of low-risk patients hospitalized for CAP and improving the quality of medical attention initially given to CAP patients in emergency departments.



Thase

Michael E. Thase, professor of psychiatry, is overseeing a large-scale study of St. John's Wort for the treatment of depression. St. John's Wort is a widely used herbal remedy for depression, yet there have been few controlled studies in this country to demonstrate its effectiveness or risks.

The University of Pittsburgh has received \$5.3 million from the National Institutes of Health to fund research into gene therapy for improving muscle function. **Leaf Huang**, professor of pharmacology and director of this multi-project grant, hopes the research will lead to treatments for hereditary diseases, such as Duchenne muscular dystrophy, as well as offer relief from common muscle injuries.

Huang also was named the Joseph Koslow Professor of Pharmaceutical Sciences at the School of Pharmacy.



Huang

Richard Simmons, distinguished service professor and former chairman of the department of surgery, appeared on the July cover of *Archives of Surgery*, after being named one of two dozen surgeons who have made important contributions to surgery. *Archives* honored surgeons for advancing research, clinical care, and surgical education. Simmons was recognized for his surgical skills, his transplantation research, and his work with sepsis. —RS

CENTURIES TURN, TURN, TURN. . .

"The main trouble. . . with the Medical School light," wrote an architect in the early 1900s, "is that all the light in the room comes from the sky-light and in Pittsburgh a sky-light. . . is no good."

PATRICIA NAGLE/CIDDE



Pitt's retired and emeritus faculty and alumni help educate new med students.

Too Good to Quit: Pitt's New Senior Mentors

Spending days, maybe weeks traveling. Visiting the grandkids. Digging in the garden. Sound like perfect ways for retirees to spend their time? Not to a handful of retired doctors; they would rather be teaching med students.

Thanks to the School of Medicine's new Senior Mentor Program, retired and emeritus faculty members and alumni, many with more than 30 years of experience, are sharing their knowledge with students.

The program, which began in the fall, is designed to help med students in a variety of areas. Mentors tutor in course work and facilitate problem-based learning sessions. But overall, they are there to provide support for both students and faculty.

The students and faculty aren't the only ones benefiting from the program; the mentors say they thrive on it. "Associating with students is stimulating," says Stanley Hirsch, MD '57, a vascular surgeon and clinical instructor in surgery. "It helps me stay on my toes."

Others just felt like something was missing. "I jumped at the chance to be a part of the program. When you retire, there are just certain things you miss, for me it was teaching," says Felix H. Miller, MD '55, an obstetrician, gynecologist, and clinical professor.

So far, six senior mentors are participating in the program. In this, the inaugural year, they work solely with first- and second-year students. But the program hopes to involve mentors in the med school's later and more intensively clinical years, so they can share their experience with students every step of the way. —SN

FOR MORE INFORMATION: Contact the school's Office of Medical Education, 412-648-8714.

President in Training

J. Nadine Gracia (MD '02) has some big plans. The first-generation Haitian American is getting her MD at Pitt and also pursuing a master's in public health. She sees herself one day working internationally. Gracia would like to do medical mission work in Haiti, for example. But first, she has her sights set on the presidency.

Last spring, Gracia was nominated president-elect of the Student National Medical Association (SNMA). "It's a very awesome and exciting responsibility," she said, reflecting on the election. The honor took a little while to really hit home. But Gracia, then a second-year med student, jumped right into her "training year" as president-elect, learning the responsibilities of being president and developing her own executive agenda. In April of 2000, she'll be installed as president.

The SNMA, the oldest and largest medical student organization focusing on concerns of students of color, seems the perfect place for Gracia, who is driven to address minority issues aggressively. "The work we do in the SNMA exposes med students to the particular health needs and concerns of under-served communities," she says.

"By working with and learning from minority communities . . . we learn how to better serve them as future physicians."



JOANNE BARTONE/CIDDE

Gracia

CENTURIES TURN, TURN, TURN. . .

"Dean of the School of Medicine recommends beginning in the Fall that two years college work be required for entrance to Medical School."

—Trustees' minutes, April 7, 1909

PITT ALUMNA IS NEW EDITOR OF JAMA

"YOU JUST HAVE TO GO WHERE YOUR HEART AND HEAD TAKE YOU," SAYS CATHERINE DE ANGELIS (MD '69). Her heart and head most recently took her from the office of vice dean for academic affairs and faculty at Johns Hopkins into the office of editor at the *Journal of the American Medical Association (JAMA)*.

There's no shortage of people who like to point out that De Angelis is the first female editor in *JAMA*'s 116-year history and the first woman to have reached the dean's office at Johns Hopkins. Her response: "I hope to live long enough so I don't have to hear, *How's it feel to be the first woman who . . .* But we are still cracking that glass ceiling. I don't mind being one of the people to help make that happen."

Someone recently said that De Angelis has one of the most influential voices in medicine, but she thinks that might be stretching it a bit. "But [*JAMA*] is a great bully pulpit," she says.

"This journal is subscribed to by 360,000 American physicians and 390,000 foreign physicians; there are publishers in 14 foreign countries. Besides America, it goes to 43 countries." And that isn't counting those



De Angelis

who read the journal online or in libraries. With this kind of readership, she helps to set the agenda for current medical discussions. She publishes papers, writes editorials, and does a great deal of public speaking. The first issues she wants

to bring to the pulpit: the plight of academic medical centers, women's health, and children's health.

"Someone once told me that all segues are intuitive. Maybe that's how I got to this point," De Angelis says, laughing.

"But I must tell you," she says, "if someone had told me a year ago that I would be the editor of *JAMA*, I would have looked at them like they were nuts."

In fact, as she packs up her office at Johns Hopkins, she says she is still trying to figure out how she got there in the first place. —RS

FOR MORE INFORMATION:
<http://jama.ama-assn.org>

Flashback

"It was 1956, three years after Sir Hans Adolf Krebs won the Nobel prize, and we'd just spent the whole afternoon learning about his discovery. . . the Krebs cycle, which describes how our bodies produce energy. After spending hours learning each individual step in the cycle, we were dazzled. Overwhelmed by the complexity. So, several fellows in the freshman class got a few cents together and sent a telegram to Klaus Hoffman that read:

'The Krebs cycle has been invalidated. Signed, The Nobel Committee.'

We did it just so we wouldn't have to learn any more of it. But it didn't work. We all had a good chuckle, then went downstairs and learned the whole thing."

—Phillip Balk, MD '59

A Quick Dose of Med School

Medical school in four months. While it isn't a possibility for people in the medical profession, it is available to those wanting to learn about the ins-and-outs of medical education.

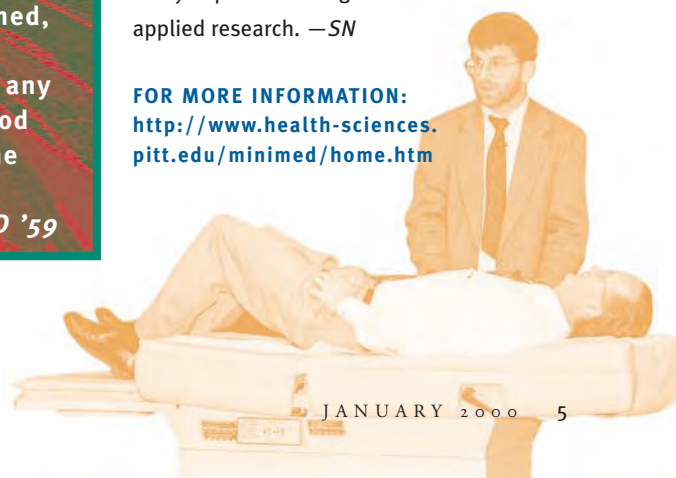
In the fall, through its new Mini-Medical School program, the University of Pittsburgh School of Medicine offered a series of free evening lectures to the public, similar to those offered to its med students. The program was designed to help the general public understand modern medicine and what medical students learn as they become physicians, says Loren Roth, "dean" of Mini-Med and associate senior vice chancellor for the health sciences.

Beyond learning about the educational

process, participants got a dose of basic information. Lectures covered topics like doctor-patient relations, human genetics, cancer, back pain, and AIDS.

Participants received certificates upon completion of the Mini-Med School curriculum. Of course, these med school graduates won't be able to practice medicine. But according to Mini-Medical School organizers, they *will* have a greater understanding of how medicine is practiced and how practice is continuously improved through basic and applied research. —SN

FOR MORE INFORMATION:
<http://www.health-sciences.pitt.edu/minimed/home.htm>





Appointments

Pittsburgh native **Joel Nelson** has returned home to head the new Department of Urology at the University of Pittsburgh School of Medicine. As the founding chairman, Nelson's mission is to enlarge and enhance the department, with a special focus on prostate cancer. Nelson oversees faculty recruitment, program initiatives, clinical and bench research, and residency programs. He was previously director of urologic oncology at Johns Hopkins Bayview Medical Center.



Joel Nelson

Nelson has considerable experience with nerve-sparing radical prostatectomy, which allows men to maintain potency after surgery. In his research, Nelson is exploring new therapies and new understandings for treating androgen-independent prostate cancer (the lethal stage). He conducts a number of basic and clinical research programs related to prostate and bladder cancer. In 1995, he unveiled the role that the peptide endothelin plays in prostate cancer and is now directing clinical trials blocking endothelin production.

Neil Resnick was appointed as the first permanent chief of the geriatrics division and a professor of medicine at the School of Medicine.

Resnick, formerly an associate professor at Harvard Medical School and chief of the Division of Gerontology at Brigham and Women's Hospital, will head the geriatric division at UPMC Health System. The division includes the geriatric training programs at UPMC Presbyterian and UPMC Shadyside, the Benedum Geriatrics Center, and the

Geriatrics Research and Education Clinical Center at the VA Pittsburgh Health System, which recently received a major grant from the

Veterans Administration for excellence in geriatrics.

Susan Greenspan, an endocrinologist specializing in osteoporosis and bone densitometry, has joined Pitt as a professor of medicine. She has a joint appointment with the geriatrics division and serves as head of endocrinology at Magee-Womens Hospital. She also is associate director of the General Clinical Research Center at UPMC Montefiore.



Susan Greenspan

Greenspan's work integrates clinical experience and research on osteoporosis to enhance the health-care system currently available to women in the Pittsburgh area. She was formerly an associate professor of medicine at Harvard Medical School and held clinical appointments at Beth Israel Deaconess Medical Center in Boston. ■

This fall, the Western Psychiatric Institute and Clinic (WPIC) was coined the Thomas Detre Hall of the Western Psychiatric Institute and Clinic. Detre, former senior vice chancellor for the health sciences, was instrumental in bringing Pitt's psychiatry program into national prominence.

CENTURIES TURN, TURN, TURN...

In 1883, the Pennsylvania State Legislature passed an act permitting the "distribution and use of unclaimed human bodies for scientific purposes."

Revising the Blueprints: A New Center for Human Genetics

"MOST PEOPLE ARE BORN WITH THE DISEASES FROM WHICH THEY DIE."

Sir William Osler, the first professor of medicine at the Johns Hopkins School of Medicine, was ahead of his time when he made that claim roughly 100 years ago. Only in the past few decades have researchers discovered just how integral a role genes play in a wide range of diseases and disorders. During those years, from Herb Boyer and Stanley Cohen, who inserted a gene into bacterial DNA and created the field of genetic engineering, to Bert O'Malley and his GeneSwitch (see story p.18), Pitt and its graduates have been fore-runners in genetic research.

The next frontier is the application of basic knowledge to preventive medicine. Medical researchers hope to identify people at risk for genetic disorders before they become symptomatic, in order to manage their condition and minimize or prevent adverse effects. But this goal of "molecular medicine" requires intensive research efforts. To keep up with scientific demands, Pitt's med school is developing one of the nation's most advanced centers for human genetic research. The Center for Human Genetics will focus on identifying clear links between genes and disease through initiatives extending from basic laboratory research to clinical application.

Until recently, the main focus of clinical genetics was testing for rare and severe genetic disorders. But genetic research has



exploded, and with it comes a new understanding of genes and their role in a wide range of human conditions. More and more it appears that changing lifestyles, medications, and in some

cases, altering genetic material can correct or minimize the consequences of abnormalities in DNA. Research in this area has only just begun, and it's one area where Pitt's proposed center will focus its efforts.

"However," notes Dean Arthur S. Levine, "in the post-genome era, genetics won't be enough: The center will also take on the much more daunting sciences of cell and structural biology, with a good dose of computational biology. The center's ultimate goal is to illuminate how the protein products of multiple genes interact at an instant in time and space."

The center will be centrally located in the Biomedical Science Tower. It will house laboratories, core facilities, and administrative offices and about 12 senior investigators, including the center's director. Projected costs total \$36.5 million over five years for faculty, facilities, and operating expenses. Administrators are planning for \$18 to \$20 million to be covered by philanthropic contributions. —RS & SN

Shirley Klinghoffer's *Strengthen* (1992), was one of many pieces showcased in the "Romancing the Brain" exhibition in October at the Pittsburgh Center for the Arts. Several Pitt med faculty members participated in the event, which delved into the mysteries of the brain in a public forum. ■



TWENTY YEARS OF CHANGE

It's 9 a.m. on a Monday and the Office of Student Affairs and Minority Programs is hopping. Students flow in and out, some to seek advice, some just to say "Hi." Many think it's the friendly atmosphere of the office that keeps the students coming back. And that's how it has been nearly every day since the office opened 20 years ago.

Getting students to come back is a high priority for minority affairs. The office started out as a way for the school to coordinate recruitment and retention of minority students. Back in 1979, the year of its inception, there were only three minority students enrolled in the medical school. Today, there are 66. As Paula Davis, assistant dean of student affairs and director of minority programs, notes: Student diversity not only enriches the learning process, it enriches the University as a whole. —SN

FOR MORE INFORMATION: <http://www.dean-med.pitt.edu/offices/minprgms/frames.htm>



DAMAGE VEILED IN SMOKE

A TEAM OF PITT RESEARCHERS DELVES INTO THE
LONG-TERM EFFECTS OF SMOKING DURING PREGNANCY.

BY MAURA MOLITOR AND REBECCA SKLOOT

At one time, Nancy Day was a smoker. Back then, she probably never guessed she would spend almost two decades studying the children of women who smoked during pregnancy and the impact nicotine has on their lives.

Day, professor of psychiatry, epidemiology, and pediatrics at the medical school, is project director of the Maternal Health Practices and Child Development Study, an ongoing study at Western Psychiatric Institute and Clinic that examines the multitude of exposures an embryo faces during development. She runs this umbrella study with Marie Cornelius

and Gale Richardson, both of whom are associate professors of psychiatry and epidemiology. Day and her colleagues study everything from alcohol and cocaine to depression and social support, and according to Day, their findings related to tobacco have been some of the most surprising and interesting to date.

Until recently, the scientific community paid little attention to nicotine exposed children as they grew into young adults. Researchers have known for years that babies exposed to nicotine are smaller when they're born, but gain all the necessary weight by their first year.

As a result, Day says, "Everyone always assumed tobacco was not a particularly serious exposure."

But with the results she and others are finding, it looks like it's time to take tobacco seriously.

For example, according to Day, "There is now some evidence that shows these kids are much more likely to develop problematic behaviors."

Day notes that nicotine may cause subtle long-term central nervous system damage

that results in children acting out early in life, and growing increasingly delinquent with age.

Day has three kids of her own, but if you count the ones in her study, she has 703. She and her colleagues are tracking these children from the womb into their teenage years and beginning to examine the role fetal environment plays in a child's future substance use. They have uncovered data that would have been impossible to detect in a shorter-term study (the children are now 14 years old).

The study indicates that at 10 years of age, 14 percent of the children who were exposed to a pack or more prenatally over a trimester had experimented with tobacco compared to two-and-a-half percent among those not prenatally exposed.

Day finds these data alarming and plans to do further research to determine what this means in relation to the general population.

If her hunch is right, then not only does smoking damage children as they grow, but it may make them more likely to perpetuate the problem in future generations by becoming smokers.

"All of these effects are imminently pre-

ventable," says Day, and that frustrates her. It seems that the solution—to quit smoking during pregnancy—is not a popular option.

Researchers find that, because of patient education, and because the body's biological tolerance for drugs like alcohol, cocaine, and heroin decreases during pregnancy, the use of these drugs diminishes as well. The only drug for which this is not true is tobacco.

"I don't know whether it's because we don't talk about tobacco during pregnancy, or because it's one of the hardest drugs to kick," she says.

"But they keep on smoking. It boggles my mind."

As Day continues to follow the development of her 700-some young participants, she hopes to create education programs to help prevent exposure in future generations.

"You have to start teaching, women and men both, that pregnancy is a vulnerable time. It's not a time to smoke or take drugs.

"We need to get that message through. We need to tell the medical personnel that this is an important issue, on a basic level, to tell women that it's not to their child's advantage to smoke or take drugs during pregnancy." ■

WITH ALL DELIBERATE SPEED

KIRKWOOD HAS DEVELOPED AN FDA-
APPROVED INTERFERON TREATMENT FOR
HIGH-RISK MELANOMA PATIENTS—AND HE
WANTS TO DO MORE. | BY KAREN LEVINE

“W e’re running out of time to get this patient approved for the new study,” John M. Kirkwood says softly yet insistently into the phone. His method is at the same time diplomatic and urgent. Kirkwood, who developed one of the most effective treatments for high-risk melanoma patients, is anxious to complete studies on the next generation of

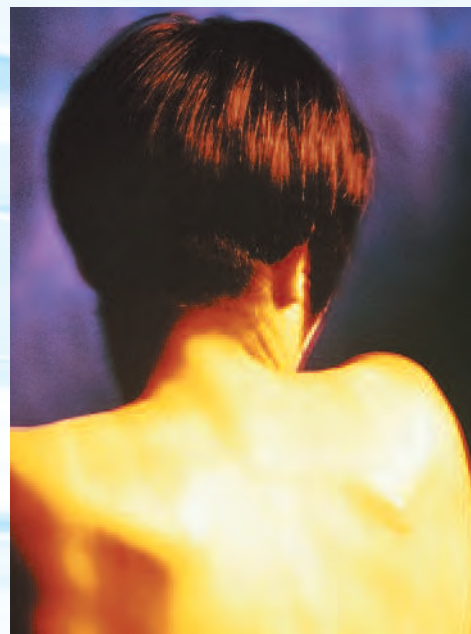


PHOTO: JISC



PHOTO: JSC

Kirkwood warns against episodic, recreational skin exposure.

therapeutics, which he hopes will prove even more successful. The stakes are high.

The incidence of melanoma, a cancer that attacks melanocytes (pigmented cells, which give skin its color) then spreads through the body in lymph or blood, is increasing. Kirkwood, Pitt professor and vice chairman for clinical research in the Department of Medicine and director of the Melanoma Center at the University of Pittsburgh Cancer Institute, offers some statistics. In the United States, deaths from melanoma have doubled from 3,600 in 1960 to 7,300 in 1999.

"Episodic, recreational sun exposure is the culprit," he says, cautioning against the burn and blister blitzes sun worshippers endure. According to Kirkwood, unlike basal and squamous cell skin cancers, no evidence exists that sunscreen offers any protection against melanoma. But that's only half the story. In the 1940s, barely 50 percent of patients survived this disease. In 1999, patients who underwent surgery for primary melanomas had an 88 percent chance of surviving for five years. Much of this, Kirkwood says, is due to early diagnosis and removal of the tumors when they're less than 1 millimeter deep.

The outlook is not as bright for those whose growths are more advanced; prognosis deteriorates as tumor depth increases. But Kirkwood is working to boost the survival rate for even the highest-risk patients.

With the Eastern Cooperative Oncology Group, Kirkwood has conducted two clinical

studies on the efficacy of interferon alpha-2b in treating melanoma. The first study included 287 patients with "deep primary tumors" whose cancer had, for the most part, spread to their lymph nodes. The worst possible cases. Kirkwood's results, published in January 1996 in the *Journal of Clinical Oncology*, reported that of the patients treated, 46 percent were still alive after five years; and 37 percent remained disease-free. At the 1999 Annual Meeting of the American Society of Clinical Oncology, Kirkwood happily reported that his second study demonstrated that the results were "real and reproducible." Of the 642 high-risk patients involved in the follow-up study, 53 percent of those treated with

high-dose interferon were alive after five years; and 44 percent were disease-free. The FDA has approved this therapy for patients at high-risk for recurrence of melanoma.

Research into biological therapies is not new. Interferon (a name popularized by the Flash Gordon comic strip to denote a substance that protects against alien infectious assault) has been around since the 1960s as an approach to treating various tumors. Yet nobody really understands what makes interferon work, although several hypotheses exist. It may alter the immune system to cause an overall increase in the body's response to antigens, or it may inhibit the tumors themselves—rendering them unable to divide and grow, or cutting off their nutrient and blood supply. The theory Kirkwood finds most likely is that interferon may activate antigenic molecules—"flags"—on the surface of cancer cells, which increase the immune system's ability to detect and attack malignant tissue. Regardless of how it works, similar to chemotherapy, interferon is toxic. The amount patients can tolerate varies, and sometimes their bodies react as though they've been hit with an intense case of the flu—a problem that causes many patients to stop treatment abruptly, before the drug has had a chance to do its job. So Kirkwood and his team are investigating alternative treatments that may be more effective with lower toxicity levels. Each trial takes a different approach: from triggering the creation of antibodies

powerful enough to protect patients from a relapse to activating cells that may destroy melanoma with greater efficacy. Kirkwood and his research team are hopeful that their trials will lead to additional important therapeutic results.

Kirkwood's ultimate goal is to find a way to immunize people against melanoma. He's working on that too, with all deliberate speed. ■

FOR MORE INFORMATION:

<http://www.upci.upmc.edu/Internet/melanoma.html>



THE TRANSPLANTATION OF A SURGEON

A PITT PROFESSOR DELIVERS
EXPERTISE TO THE MEDITERRANEAN
BY REBECCA SKLOOT



ABOVE: Palermo, Italy
LEFT: Marino

When the Italian government got word that a liver was waiting in Pittsburgh for five-year-old Sophia (not her real name), they loaded her onto a military plane bound for overseas. It was 1992. Southern Italy didn't have the technology to help her, so the government had to get Sophia to her new liver. And fast.

When she arrived at Pitt, Ignazio Marino stood waiting. As he ran with the gurney from the ambulance to the elevator, Sophia lay still, frail, understanding the situation all too well. The first time she met Marino she was less than a year old. He was the nice man who gave her her first new liver. Since then she'd seen Marino for almost one transplant a year. As they rode the elevator toward the operating room, Marino and his colleague Andreas Tzakis began preparing her for surgery. Sophia's new liver had been waiting more than eight hours while she crossed the Atlantic; there was no time to spare.

In 1995, the Italian government spent in excess of \$250 million sending its citizens abroad for organ transplants, says Marino. Still, in Sicily alone, about 2,200 each year die from liver disease.

According to Marino, professor of surgery at Pitt, "If people don't develop resources in other countries, when they need organ transplants they will have just one option: dying."

This is why UPMC Health System, in collaboration with the Italian government and two Palermo hospitals, has broken ground for construction of a 70-bed multi-organ transplant facility in Palermo, Sicily. The new Mediterranean Institute for Transplantation and Advanced Specialized Therapies, also known as ISMETT, is headed by Marino.

Italians aren't the only ones who benefit from the new facility. Says Marino, "It puts this knowledge and science at the service of the Mediterranean area: North Africa, the Middle East, Turkey, Egypt, and other countries."

Marino speaks with pride of the international patients he was able to save in Pittsburgh: "Many of them now live wonderful lives—better than mine!" Other patients serve as daily reminders and fuel the sense of urgency in his work.

Standing in the Pittsburgh airport in late summer, awaiting a flight overseas to begin his work at ISMETT, Marino spoke softly into a pay phone as he told the story of Sophia.

"She didn't make it," he said. "And I always thought that maybe if she. . ." His voice trailed off.

"[Sophia] lived five years. But if she could have, you know, had a transplant service close to home, and wasn't dependent on one across the ocean, maybe she would still be alive."

"I think I need to go," he said after a long silence, "otherwise I will be left in Pittsburgh."

After hanging up the phone, Marino boarded his plane, and within days performed the first-ever liver transplant in Sicily. ■

FOR MORE INFORMATION:
<http://www.ismett.edu>



Cortisone crystals

ALUMNUS PHILIP SHOWALTER HENCH'S PATH TO THE DISCOVERY OF CORTISONE, AND THE NOBEL PRIZE

BY REBECCA SKLOOT

SUBSTANCE X

Packed shoulder-to-shoulder beneath the chandeliers of the Waldorf-Astoria ballroom, hundreds of physicians fell silent as Philip Showalter Hench (MD '20) was about to speak. He had avoided this moment until he was sure his research findings were solid. Rumors were stirring. Someone heard Hench had discovered the cure for rheumatoid arthritis. It was time to set the record straight.

It was 1949, a year before he would share the Nobel prize, when the University of Pittsburgh School of Medicine alumnus turned to his audience to introduce a drug that functioned in a way they had never imagined. It didn't kill germs, like penicillin, nor did it replace hormone deficiency, like insulin. It actually changed a patient's body, enhancing its ability to resist inflammation and repair injured tissue. Hench's story spanned more than 20 years but came to a head only one year before, in 1948, when a patient refused to leave his office.

Jean Olsen (not her real name) came to Hench when she couldn't take it anymore. She'd been an outpatient at the Mayo Clinic, where Hench directed the rheumatology section. Olsen's joints were deteriorating. Her right hip splintered after her 25th birthday, and at 29 she could not trust either leg for support. She came for relief, she told Hench, and wasn't leaving until she got it. She demanded to be hospitalized. Though Hench resisted, Olsen's insistence came at an opportune time. He was onto something. He and a colleague, Edward C. Kendall, were doing some research, and Hench thought they might have found a treatment for rheumatoid arthritis. This treatment, a substance they called compound E, was an adrenocortical hormone so precious it took three thousand pounds of beef adrenal glands to make one gram. No one had ever



Hench

given it to a patient with rheumatoid arthritis. But with Olsen waiting in a nearby hospital bed, Hench was determined to try. So he wrote a letter to Merck & Company, Inc., the one laboratory that had managed to manufacture it, and asked for several grams of compound E.

Olsen was at the point where she could not hold a cup, lift a spoon, or comb her hair. When she awoke the morning of her first compound E injection, she couldn't get out of bed. The next day, still no change. But within a few days, she rolled over painlessly, jumped out of bed, and felt like, well, shopping. Olsen was a new woman with a new body—she wanted to dress it up.

The drug's real name was 17-hydroxy-11-dehydrocorticosterone, but Hench resisted calling it that. "Can you blame me?" he asked, "I can hardly pronounce it." Hench had a cleft palate he fought to overcome, but its effects lingered. Sometimes he couldn't say complex words, and his speech came out muffled. So Hench and Kendall dubbed the drug "cortisone." After seeing its effects on Olsen, Hench gave it to four more patients, with the help of colleagues Charles Slocumb and Howard Polley.

PHOTOGRAPHY | ARCHIVES OF PHILIP KAHLER HENCH (MD '58), THE MAYO CLINIC, MERCK & COMPANY, INC., AND THE UNIVERSITY OF PITTSBURGH ARCHIVES



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"I got sick of having to wash my face with a dripping cloth," one patient said. "You see, I couldn't

wring it out." She opened doors with her elbows and used her teeth to pull blankets over her body. Hench began compound E injections and everything changed. "I just threw off the covers and jumped out of bed," she said. "I felt so good that I walked across the room on tiptoes—the first time I'd been able to do that in years." She washed her face, wrung the cloth, and a few days later climbed hills behind the hospital, "just for fun."

Thanks to cortisone, the inflammation in these patients' joints decreased; and with it went their pain. The results were liberating—at first. But the excitement didn't last. There wasn't enough compound E for Hench's five patients, let alone millions, but that wasn't the real problem. There were side effects.

Olsen's reaction to the drug came quickly. Her face grew pale and swelled like the moon. Her periods stopped. Some days she gained four, maybe seven pounds. But Olsen wasn't the only one whose body went haywire. Some of his trial patients were overtaken by euphoria, others by psychosis. They became dizzy and disoriented. Their blood pressure fluctuated as rapidly as Olsen's weight. Hench lowered their doses and the pain flooded back, yet he was confident he had found a tool for understanding rheumatoid arthritis.

"Cortisone," Hench said, "is the fireman who puts out the fire, it is not the carpenter who rebuilds the damaged house." It wasn't the cure, but by studying how cortisone worked, he hoped to find something that was. He believed it existed; because he thought he'd seen it in action.

April Fools' Day in 1929, 20 years before his presentation at the Waldorf-Astoria, Hench walked into a Mayo exam room expecting to see yet another patient with rheumatoid arthritis. What he

found instead, a limber man with skin the color of dried lemon, was unlike anything he'd ever seen. This, he thought, had to be a joke.

"Where is this rheumatoid arthritis?" Hench asked.

"I had it last week," the man replied, "but when the jaundice came on it disappeared."

Impossible. Rheumatoid arthritis was irreversible, everyone knew *that*.

As the patient told his story in that exam room on April Fools' Day, Hench absorbed every detail. The man hadn't lifted his arms above his head in years. He couldn't. And when he could walk at all, the effort was just shy of unbearable. Then his skin turned yellow. The next day, the pain and swelling in his joints disappeared—he threw his hands over his head and for the first time in years, nothing hurt.

Jaundice occasionally was a problem for patients with rheumatoid arthritis; it was a

suddenly, thanks to their failing livers, they felt alive for the first time in years. Those who survived their jaundice eventually returned to their arthritic state. Though many colleagues thought he was running blind, Hench couldn't shake the feeling he was onto something. It was clear, liver disease stimulated the body to produce a therapeutic substance, one he called "substance x." He just had to find it.

Hench started infusing human bile into the stomachs of volunteer patients with rheumatic disease. He had a hunch. If he could induce jaundice, he could study how it relieved pain. He infused these volunteers with jaundiced blood, gave them ox bile in olive oil, and though some became jaundiced, in the end, the experiments relieved no pain.

After these experiments failed, he started a second "collection." In 1931, Hench

Suddenly, thanks to their failing livers, they felt alive for the first time in years.

potentially fatal side effect of cinchophen, an antirheumatic. Many of cinchophen's jaundiced victims felt relief from arthritic pain, and most assumed this was cinchophen's doing. But Hench's yellowed patient never took cinchophen, or any other drug; still his pain vanished. *Perhaps*, Hench thought, *it's jaundice that relieves pain, not cinchophen*. For rheumatoid arthritis, a disease with no known cause, any hunch was worthy of pursuit.

Some called it compulsion, others called it passion, but Hench was driven by a desire to collect anything from which he could learn. Hench began "collecting" jaundiced patients with arthritis in 1929. All but two had taken cinchophen, and most were dying from the jaundice it induced.

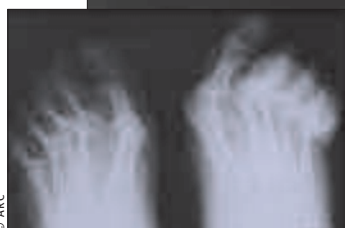
Each patient came to Hench with a similar story: Their joints had deformed. For some, it was so bad their fingers and toes curled, and they couldn't dress or use a toilet alone. Then

saw a pregnant patient with rheumatoid arthritis whose story echoed that of jaundiced patients. He sought others, and found many with similar histories: Deteriorated joints left them unable to manage their housework or care for their children, unless they were pregnant. After poring over patients' stories, Hench realized substance x wasn't a liver by-product at all. It was something stimulated by physical stress. The goal, as Hench saw it, was to find a common chemical denominator—something that explained how two otherwise unrelated conditions, jaundice and pregnancy, lead to a common outcome, the relief of rheumatic pain. To Hench, the most likely explanation was hormonal. It made sense that jaundice and pregnancy, with the stress they put on the body, could tweak some gland into producing extra—or different—hormones.

COURTESY PHILIP KAHLER HENCH AND THE MAYO CLINIC



Edward Kendall (in sweater) and Philip Hench (far right) with colleagues Charles Slocumb (left) and Howard Polley in Kendall's laboratory at the Mayo Clinic



But he had no idea which hormone. He needed a chemist.

Edward Kendall, a soft-spoken biochemist at the Mayo Clinic, had worked on the same campus as Hench for years; but the two hadn't talked much. Back in 1929, the year Hench started collecting jaundiced patients with rheumatoid arthritis, Kendall began studying the adrenal gland. By 1938 when Hench approached him, Kendall had identified six adrenal hormones. He named them compounds A through F.

With their first conversation about adrenals, Kendall was wary. He didn't know much about arthritis, and he didn't want his work with Hench to interfere with his adrenal research. But he gave it a chance and grew intrigued by the project. Other Mayo researchers would soon become accustomed to seeing Kendall and Hench together, leaning back in wooden chairs, feet propped on a radiator, deep in thoughtful conversation. The two spent endless hours pondering Hench's

ABOVE: Edward Kendall (left) and Philip Hench (right) at the Mayo Clinic.

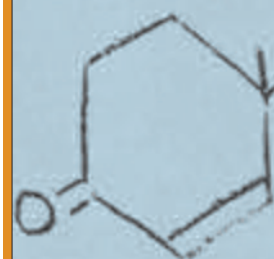
BELOW RIGHT: A Merck scientist explains the crucial experiment for the synthesis of cortisone.

question: *What the devil could this mysterious substance x be?* Kendall and Hench pondered and hypothesized; but little did they know, a few yards away in his lab, Kendall was isolating substance x. He called it compound E.

In 1941, Hench and Kendall agreed to try compound E on a patient with rheumatoid arthritis. The reasoning was fragile at best, but seemed somehow logical. Hench had noticed that reactions to typhoid vaccines gave rheumatic patients pain relief. These remissions were freak events, but Hench kept track of them.

One day, Kendall mentioned compound E. He had separated it in tiny amounts and discovered that it made some animals resistant to typhoid vaccine reactions. To Hench, this was as good a connection as they'd seen. The two men decided it was worth a try but had no idea it would be almost eight years before they would have enough compound E to follow through on their decision.

With a chemical structure more complex than any molecule ever reproduced in a laboratory, compound E had Kendall stumped. He needed the help of a pharmaceutical company. But because of the compound's complexity, and merely a hunch about its value, there was little motivation for production. Later that year, as the war in Europe escalated, there was talk that submarines left Germany empty and returned full of Argentinian beef adrenal glands. Rumor had it German scientists had found an adrenal hormone they injected into fighter pilots, making them more resistant to oxygen deprivation so they could fly at inhuman heights. Suddenly, adrenal hormones became interesting.



The U.S. government called a special conference on adrenal research, and adrenal hormones became a top national priority.

Though the rumor of German hormones soon died, it began a heated race toward compound E. It was 1948 when Kendall and Merck produced the first dose. But Hench had none, and Jean Olsen was refusing to leave the hospital. Beyond Olsen, there were many like her who needed relief; he believed compound E could provide it. So Hench sat down and wrote the letter to Merck asking for a few grams of compound E.

In 1950, one year after his presentation at the Waldorf-Astoria, Hench found himself in Sweden, sitting next to William Faulkner, staring in awe at trumpeters on marble stairs, as he, Kendall, and Tadeus Reichstein (a chemist who mastered some of the essential steps in cortisone's synthesis) waited to accept their Nobel prize for the discovery of cortisone and its clinical applications.

Cortisone is not a cure for rheumatoid

arthritis. Medical science is still searching for that miracle. But cortisone is a therapeutic for rheumatoid flare-ups. When he accepted his Nobel prize, Hench urged everyone to be patient and not rush to prescribe cortisone before they understood its dangers, limitations, and uses.

Later, investigators illustrated the tremendous capabilities of cortisone: It could save an asthmatic whose airways collapsed suddenly, correct fatal hormonal imbalances, cure the maddening burn and itch of skin diseases, and much more.

Without Hench, cortisone would have been discovered, but its clinical value might have stayed hidden for years.

Hench simply refused to abandon his belief that our bodies are capable of producing a mysterious antirheumatic. He praised his colleagues in academia and industry, for without them, Hench once noted, he "would have been like a Columbus, sitting on the seashore, yelling futilely that the world was round, and nothing would have happened." ■

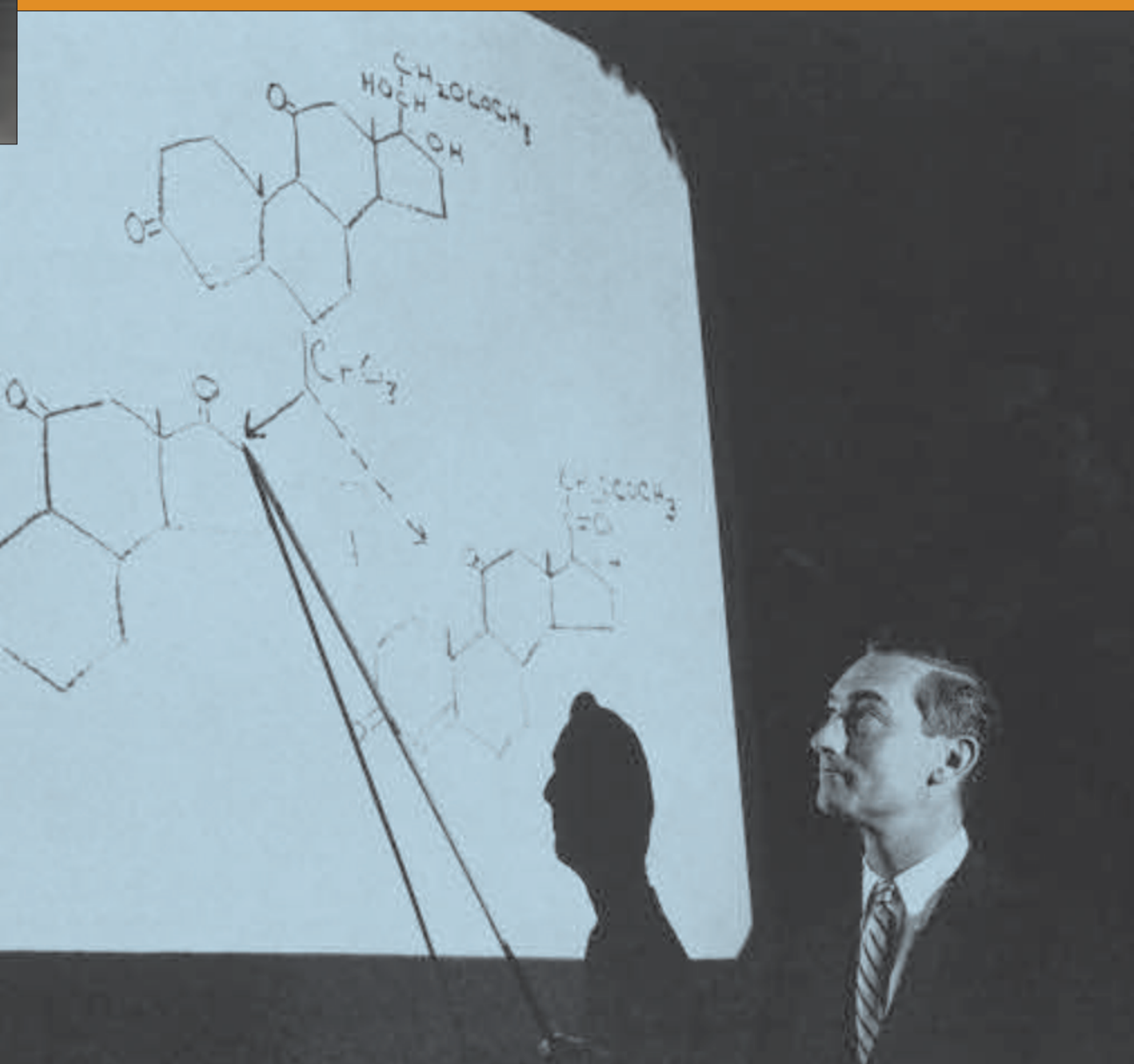
A LIFELONG INJECTION

Professor Christopher Evans and associate professor Paul Robbins, both of the University of Pittsburgh School of Medicine's molecular genetics and biochemistry department, recently completed the first-ever arthritis gene therapy trial. Their technique utilizes a gene whose product blocks interleukin 1 (IL-1), an agent which stimulates joint inflammation. The idea of suppressing inflammation in joints is not new; physicians have been using cortisone and other steroids to do this since Philip Hench announced his startling findings. However, the therapeutic effect of steroids is short-term and side effects of prolonged therapy can be serious. In theory, says Robbins, once a gene is delivered to a joint, it could stay there indefinitely. And to date, Evans and Robbins' gene therapy has produced no detectable side effects.

The recent trial, a phase one study to evaluate safety, was, as Robbins says, "a first step." The goal now is to develop an effective therapy that can be injected into a patient's joints in any rheumatologist's office. —RS

FOR MORE INFORMATION:

<http://www.pitt.edu/~rsup/mgb/robinslb.html>





Alumnus Bert O'Malley
has changed the field of
hormone research.

LANDMARK HORMONE RESEARCHER DELIVERS THE
UNEXPECTED, SOMETIMES WITH A RUBBER CHICKEN.

BY REBECCA SKLOOT

THE SWITCH

Bert O'Malley (MD '63), hailed as a pioneer among hormone investigators, published one of his most widely reprinted papers in jest. After a department party, he and a postdoc joked about using leftover Baileys Irish Cream to clean the nonspecific radioactivity off their equipment. Usually labs would order a protein mixture from a distributor, apply it to their equipment, and the radiation came off clean. *But what if, O'Malley's postdoc asked, what if the protein in Baileys worked just as well?* Next thing they knew they'd published, in a scientific journal, a paper called "Irish Cream Liqueur as a Blocking Agent in DNA Dot Blots." Within no time it placed among O'Malley's most sought after papers. Researchers tried to buy Baileys through their purchasing offices, but administrators didn't believe it was a laboratory supply. They needed a copy of O'Malley's paper to make it legit. Of course, it wasn't. The liqueur actually worked, but made for an expensive lab soap. (Though it tasted better than most other detergents.) The whole thing was just a joke. But jokes, for O'Malley, are an essential part of how he approaches science.

PHOTOGRAPHY | PAM FRANCIS



O'Malley, pillar of the scientific community of hormone researchers, with fish

"You can have a lab where people are extremely serious but still have time for practical jokes," says O'Malley. "You've got to maintain some levity. Otherwise it becomes too pressurized."

So O'Malley never punishes a harmless prank—even if it's at his own expense.

On St. Patrick's Day, hundreds from Baylor College of Medicine gathered to celebrate. Before the party hit full force, O'Malley's colleagues had an announcement to make. The music stopped, everyone gathered around, and Bill Brinkley, vice president for graduate sciences at the college, told the story of O'Malley, the great fisherman and hunter. His prize buck was a magnificent beast, he told them, with a set of antlers that would put other hunters to shame; and O'Malley bagged him alone. Brinkley stood beneath a mounted package

saying he hoped the buck would long hang in the great doctor's office. O'Malley was pleased. The hunter approached his buck and a hush spread through the room. He grabbed a corner of the wrapping paper, ripped it open, and the crowd collapsed with laughter as O'Malley stared into a deer's hind end. An old friend, William Schrader, then the assistant dean of the graduate school, yelled "Gotcha!" Without a blink, O'Malley turned to Schrader, said "You're fired," and both men laughed.

"Science is a field where most things just don't work," says O'Malley, who developed the cell biology department at Baylor College of Medicine in '72 in the midst of a research career that changed the face of endocrinology. "You have to be a gambler. You have to not mind losing, and go for

the big win." Those who know O'Malley say if he believes in something, he'll stick his neck out for it. (And if it's football season, everyone knows they can count on O'Malley to bet on the Steelers.)

During the '70s, O'Malley discovered how steroid hormones work. Using progesterone, he showed that all steroid hormones function through a pathway that starts when the hormone enters a cell and finds its receptor and ends when the hormone reaches its nuclear gene and turns it on.

After figuring out that hormones control certain genes, O'Malley was the first to isolate a hormone-regulated gene. He showed it to the world saying, "We now know what a gene looks like." More importantly, he cloned it, showing it was finally possible to reproduce genes. The next step was to put them into ani-

mal cells to try to replace defective genes.

Once he discovered the steroid pathway, O'Malley's achievements avalanched. He would go on to isolate and purify the first steroid hormone receptor (for progesterone); discover how steroid receptors work molecularly; receive several honorary doctoral degrees, including one from the Karolinska Institute (after snagging a bite of dessert from the president's plate); uncover how receptors, and therefore the genes they regulate, turn on and off; and introduce the endocrine world to molecules called "co-activators."

O'Malley likens co-activators to stereo amplifiers. They are the system's power-boosters.

"Say hormones are the electrical signal coming into the stereo," he explains. "The receptor would be the transducer, and the amplifier would be the co-activator. You can

efforts succeeded. A mutated gene can be replaced with a healthy one, but the problem is, once the new gene is in place, it can't be turned off. Typically, genes are carefully tuned to produce specific amounts of proteins for specific actions in the cell. "If you produce just the right amount," O'Malley explains, "that's great. If you produce too little, of course, that's a genetic disease. And when you make too much, that causes other problems."

Given the fact that genetic diseases due to "overproduction" result from only a 30 percent increase in gene product, inserting a gene that never stops producing could cause monumental problems, says O'Malley. This is where the GeneSwitch comes in. The switch itself is a mutated progesterone receptor, and it's controlled by very low doses of mifepristone, otherwise known as RU-486. When

courses, delivers guest lectures around the world, and chairs one of the top molecular and cellular biology departments in the country. He gets home around 7:30 pm. "I've got a real wonderful, understanding wife," he says. His wife, Sally, helps keep him together so he can be a husband, father, grandfather, and scientist.

Until his junior year of med school, when he worked in James Field's lab at Pitt, O'Malley had never contemplated a career in hormones, or research for that matter. But once he got into the lab, O'Malley fell in love with research. If you ask O'Malley where hormone science is going, he chuckles.

"There were only 25 people in this field when I started," he says, "now there are more than 5,000 just working on one nuclear receptor. . . and there are 50 to 100 nuclear receptors. There's going to be a tremendous payoff for clinical medicine in the future. We *will* cure and, perhaps more importantly, prevent many of today's diseases." But all this will only come by understanding first, applying second.

"You have to understand how the cell works to understand the nature of disease," says O'Malley; and he believes this basic research is paying off. "It's being applied," he says. "It's being used to translate research into clinical usefulness."

But to do this translating, it takes the creativity to imagine what *could be*. And for imagination to thrive in O'Malley's world requires humor. This is why, on the wall of his private office bathroom, his buck's rear hangs proudly, with the head mounted in the next room. If you pass his office, and if the door is open, you'll see O'Malley's deer. It's jumping straight through the wall of his bathroom, into the office where O'Malley sits, at 5:30 am, thinking about science. ■

FOR MORE INFORMATION

<http://adams.bcm.tmc.edu/gradprog.html>

"Science is a field where most things just don't work."

get the signal in and get it changed into sound, but if you don't have an amplifier, you can't hear it." Just as the amplifier orchestrates signals into desired sound, co-activators guide the events of gene regulation so they produce the right gene products, in the right amounts.

But the story isn't that simple. As it turns out, different people produce different quantities of co-activators; so the same amount of a hormone can create drastically different results, depending on the person it's in. With a hormone for, say, height, if two people have the same amount of steroid hormones for growth, the person with more co-activator will grow taller than the one with less. The height issue isn't usually life threatening; but in other cases, like an excess of prostate co-activators, even a small amount of hormone could end with overstimulation and cancer. So O'Malley is trying to figure out how co-activators work. If he succeeds, he may be able to control them or compensate for their excess. He and his colleagues have already done something similar. They invented a switch to turn genes off and on at will.

O'Malley holds 12 patents, maybe 15, he can't remember. One is for the GeneSwitch, which may contribute greatly to the future of gene therapy research.

At first scientists focused their gene therapy efforts on one question: *How can we deliver a gene into the body?* By and large, their

mifepristone is present, the switch is "on" and the gene is active. When mifepristone is removed, the gene turns off. The switch and the gene it regulates are delivered via an inactivated virus or by direct injection into muscle. Though it hasn't been tested in humans, O'Malley's GeneSwitch has been regulating genes for two years and counting. It's still functioning well in the original animal models. Clinical trials, which will most likely test anti-cancer genes, are set for the end of 2000.

Someone should patent O'Malley's drive. He's at the gym by 4 am; in the office by 5:30 so he can think about science until about 7:30, when everyone else gets there; then he works with students and postdocs, attends committee meetings, teaches in three

RECEPTOR RESEARCH AND NEW CANCER THERAPEUTICS

Many cancerous cells, like those found in breasts and prostate glands, thrive on hormones. Perched on the walls of these cells are receptors, which bind steroid hormones through the mechanisms originally described by Bert O'Malley (MD '63). When the correct hormone binds the receptor and enters the cell, the cancer is fed and allowed to grow. But if the receptor is blocked, the hormone can't enter the cell and, more often than not, cancer growth is inhibited. This is precisely the mechanism behind several current cancer therapies which, when used in combination with a primary treatment (like surgery), can extend a patient's life significantly.

—RS



MASSIMO TRUCCO MAY BE ON THE CUSP OF A VACCINE

FOR JUVENILE DIABETES. | BY ERICA LLOYD

EXTRAORDINARY LIMITATIONS

It was Massimo Trucco's first invitation to speak at a scientific seminar. 1976. The young Italian physician hesitated. The international audience would expect papers to be presented in English, and Trucco didn't know a word of the language. But he decided to go after all and had his presentation translated into English; then he memorized it. Every word. Trucco reassured himself: At least he could not be expected to respond to any criticisms or questions about his work. After the talk, he could forget this research business and return to his new job as "a substitute emergency room pediatrician" at a children's hospital in Turin, Italy, building a life with his wife of two months.

Trucco closed his presentation as planned, with a smile and a shrug, saying he would like to invite questions, though because of his difficulties with English, well. . . But an elderly man sitting in the front row raised his hand anyway. In impeccable Italian, the man asked Trucco to clarify a point, proclaimed that he agreed with the thesis, and invited him to join his lab, in Cambridge.

The glitch in Trucco's plans was César Milstein, a brilliant immunologist from Argentina. Trucco not only had to account for his thesis to Milstein, as years went by, he found himself in the spotlight of the scientific community again and again. At that 1976 seminar, Milstein was intrigued by Trucco's proposal for a novel way to suppress the immune systems of organ transplant recipients, a thesis based on data he collected while on a fellowship at the University of Turin. Trucco is now a professor of pediatrics and pathology at the University of Pittsburgh School of Medicine and head of the Division of Immunogenetics at Children's Hospital, where he also holds the title, Henry L. Hillman Professor of Pediatric Immunology. These days, Trucco is fundamentally changing the way medical science understands type I, or juvenile, diabetes. His investigations into a possible vaccine and cure for the disease keep the likes of Thomas Starzl calling.

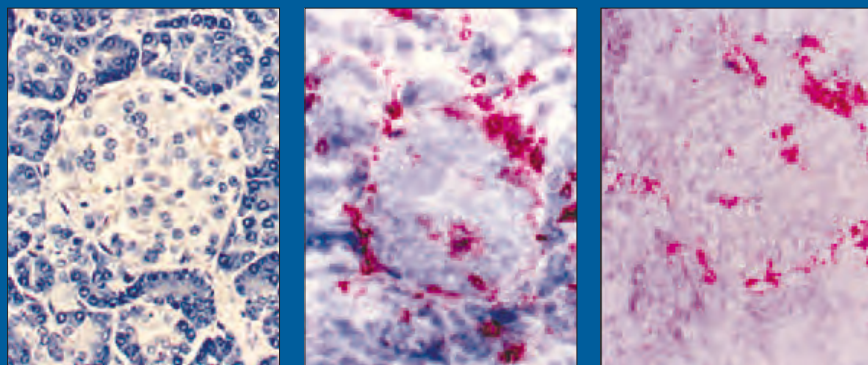
Trucco did go to Cambridge, where he could work with monoclonal antibodies, that is antibodies created to target only specific antigens. He thought, maybe he could use these monoclonal antibodies to confuse the immune systems of transplant recipients into not recognizing antigens from donor organs—organs their bodies might otherwise reject. Trucco believed his proposal would make more sense if he could manufacture antibodies *in vitro* as Milstein had just demonstrated to the scientific community.

At Cambridge, Trucco's hesitations about pursuing his research vanished.

"That was an unbelievable experience," he says. "I remember there was a tea time around 4:30, and one evening I was sitting at a table with seven Nobel prize winners." The trim, bearded 51-year-old shakes his head and laughs as he talks. It seems he still cannot believe he was ever there.

At Cambridge, Trucco was a visitor solely dependent on Milstein's graces; he had no official position. Milstein, encouraged by Trucco's work, arranged for him to continue on at the Basel Institute for Immunology in Switzerland. The esteemed and well-funded institute would offer Trucco the resources he needed to continue his project. But first, Trucco would have to endure another nail-biting seminar. Niels Jerne, the legendary head of Basel, said he would take in Trucco

PORTRAIT PHOTOGRAPHY | JULIA MAROUS STRAUT



FROM LEFT TO RIGHT: A normal human pancreas, and two views of an islet from a diabetic patient in which T cells (stained red) move in to destroy insulin producing beta cells

under one condition—in three months he would have to come up with something remarkable.

Precisely three months later, Jerne's secretary notified Trucco that he should put together a presentation for the next day. Trucco did as asked, including the remarkable part. He reported his findings: Monoclonal antibodies could indeed be used against white blood cell antigens in humans. This meant labs throughout the world could standardize immunosuppression techniques and create more precise donor matches, effectively widening the donor pool for kidney and bone marrow transplants. Throughout the presentation, Jerne smoked hand-rolled cigarettes while studying this energetic, young Italian. At the end, he sized up Trucco with a curt announcement: "Your English stinks! But your science is great. Laboratory Number Nine."

In Laboratory Number Nine, Trucco kept good company. Again, many of his neighbors were Nobel laureates. In fact, it appears most of his mentors eventually took the prize. Milstein, of Cambridge, joined the club in 1984 for his discovery of the principle for production of monoclonal antibodies; Jerne won the same year for his theories on the development and control of the immune system. Like these men, Trucco set high standards for himself.

As years went by, Trucco would father

three children (the eldest daughter now attends Pitt's med school); work again in Turin and later at the University of Pennsylvania; and at some point along the way, send his family on a two-month vacation while he "transformed himself into a molecu-

At the end, Jerne sized up Trucco with a curt announcement: "Your English stinks! But your science is great. Laboratory Number Nine."

lar biologist." His interest in molecular biology opened opportunities for cross-fertilization and more remarkable findings, including revealing how genes that encode molecules that lodge peptide antigens are organized. Eventually, another seminar would take him to Pitt. This time Allan Drash, emeritus professor of pediatrics at the School of Medicine and former director of endocrinology at Children's Hospital, was in the audience.

In 1987, Drash, with former senior vice chancellor Thomas Detre and Ronald Herberman of the University of Pittsburgh Cancer Institute, recruited Trucco to come to Pittsburgh, where his contributions have been worthy of national headlines. Shortly after arriving here, Trucco contributed to our understanding of "natural killer cells," which

target cancerous tumors. Today, many believe he is on the verge of developing a vaccine for juvenile diabetes.

Talking to Trucco these days, it can be hard to keep up. His mind races at about the speed of a Maserati. To make matters worse, if he can't think of the English word for something, he just moves on to the next idea. Besides that, there are about a dozen projects in the hopper at any time, some of which could lead to cures or vaccines for autoimmune and heart diseases. Right now he's in the midst of intense and promising collaborations with Joseph Glorioso (gene therapy) and Thomas Starzl (transplantation of insulin-producing cells). And, by the way, he also runs one of the nation's top two bone marrow donor matching centers, which gets about 1,000 blood samples to screen a day, seven days a week, 52 weeks a year.

It's hard to imagine this physician was once ambivalent about his research. In fact, Trucco has managed to surrender many of the distractions that he believes might otherwise get him off track. Wherever possible, he keeps his life simple. He owns 17 black polo shirts, 17 pairs of black Levi's 501 jeans, and a few pairs of the same brown leather Italian walking shoes. This is what he wears to work. *Every day.*

The man receives millions in grants to fund his large research operation, yet he

swears he does not know how to write a check. His wife, accomplished gynecologist and pathologist Giuliana Trucco, and his administrative assistant, Patrick Hnidka, handle such issues. Giuliana Trucco even pays his espresso tab at the local café each week. Trucco doesn't like to drive; he "has some problems making gasoline," as he says. So he doesn't pump gas, not since an unfortunate incident which resulted in Super Unleaded being sprayed all over a BP island and Trucco learning several unflattering English words from an irate gas station attendant.

But Trucco more than survived this and other immersion language lessons. It's okay, he'll say with a chuckle. He just concentrates on what he knows he can do. Some of what Trucco can do: cook soul-fulfilling dinners for

his family, fire a clay bowl, and solve a few of the mysteries of the immune system.

The black wardrobe is not just an effort to simplify. As Trucco puts it, he once made “a silly mistake—something personal, not the work.” So he makes himself wear humble black garb daily, as his way of not letting himself forget that mysterious blunder.

“I believe everyone should get a second chance, and I don’t want to blow mine,” Trucco says.

It seems much of Trucco’s work is about creating second chances, a vocation he pursues with reverence. His mission these days is the pursuit of a vaccine for juvenile diabetes. Trucco is determined to help hundreds of thousands of people avoid daily insulin injections and the complications that often result from juvenile diabetes, including blindness, kidney failure, stroke, gangrene, heart disease, and impotence.

But first he has to nail down the cause. He has done a lot of the legwork already. Shortly after coming to Pittsburgh, Trucco determined that juvenile diabetes is inherited; but not everyone who is genetically susceptible gets type I diabetes. For example, Trucco found out that in Allegheny County, about two percent of the population is predisposed and 16 percent of those people end up with the disease. So a big question remained: *What triggers the immunological reaction that stops the pancreas from producing insulin?*

There had been plenty of speculation, perhaps something to do with mother’s milk, cesarean sections, or a virus; but no one knew the answer—that is, no one knew until Trucco stayed at work late one Friday night. That night, in 1992, a boy in a diabetic coma had been rushed to Children’s Hospital from Washington, Pennsylvania. The child’s brain had swollen to the point where it had strangulated his cerebellum. He was brain dead; there was no way to save him.

The parents approved a pancreas donation and Trucco and his wife put together a team at Children’s to perform an autopsy and examine the organ at the cellular level. A microscopic view at this critical stage might offer a clue. Yet the team had to work quickly, or enzymes would flood the organ and the researchers would see nothing.

“This was the first time I had in my hands a human pancreas while the diabetes was exploding,” says Trucco.



ABOVE: Trucco in his Rangos laboratory with fellow researcher Massimo Pietropaolo (center) and technician Susan Pietropaolo. BELOW: At home with Giuliana

It may have been the first time anyone had. In the boy’s pancreas, Trucco’s team saw immunological signs of the possibility of super antigens. These hyperactive-antigens were stimulating the pancreas’s T cells to attack the beta cells within the islets. In other words, they were not allowing the pancreas to produce insulin.

The super antigens were key—they are found predominantly in viruses. Trucco had his answer.

By 1994, Trucco knew that a viral agent was likely to be responsible for juvenile diabetes; he was determined to find out, *what virus, or viruses?*



PITTSBURGH’S NEW DIABETES INSTITUTE

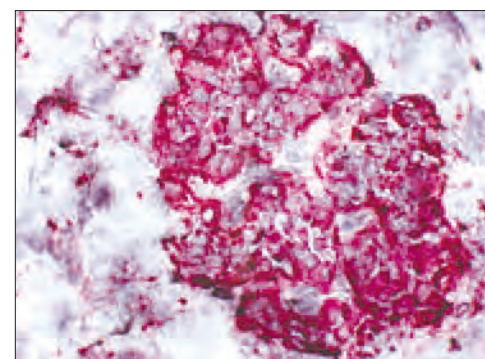
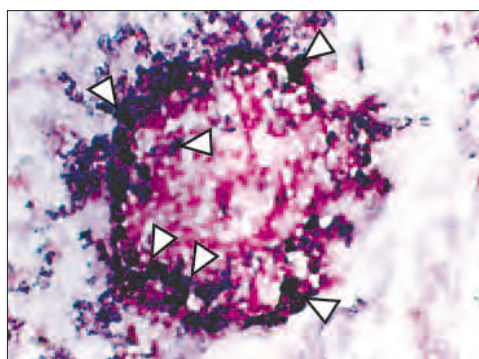
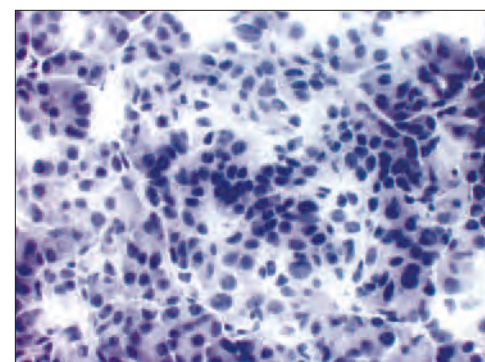
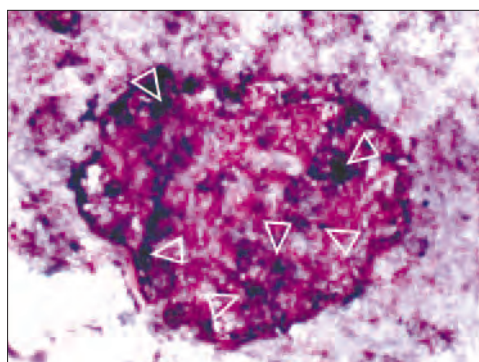
With 1.1 million diabetics in Pennsylvania, news of the University of Pittsburgh Diabetes Institute has met with open arms. According to Massimo Trucco, the institute’s codirector with Andrew Stewart, Pitt researchers have launched some of the most exciting diabetes initiatives to date; the new center will provide the space and funding for these and other projects to flourish. It will also help researchers expand their investigations and work with clinicians to deliver top-of-the-line care to diabetic patients throughout the region.

Through a joint effort of the University of Pittsburgh School of Medicine, UPMC Health System, and Children’s Hospital of Pittsburgh, renovation for the center began in November. The center is scheduled to open its doors this May. —RS

Trucco found out, thanks to a friend, surgeon Pedro del Nido, who is now at Harvard. In '96, del Nido enlisted Trucco to examine tissue from a heart transplant patient who suffered from myocarditis. Trucco found the same T cell activity in the heart transplant tissue as he had seen in the diabetic boy's pancreas. Del Nido's patient was known to have coxsackievirus B (CVB), which Trucco and others had suspected was linked to diabetes, but weren't sure how. CVB usually does no more than induce sniffing and flu-like symptoms. The tissue sample from del Nido's transplant patient indicated that certain strains could also trigger heart disease and juvenile diabetes in those who are susceptible.

CVB is a common virus that spreads through day cares and kindergartens everywhere. It all made sense. Throughout his pediatric career, Trucco had heard mother after mother say, *My child was fine until he got sick that day, then the diabetes came.*

Yet CVB is always mutating, so it would be impossible to create a lasting vaccine for it.



By 1994, Trucco knew that a viral agent was likely to be responsible for juvenile diabetes; he was determined to find out, what virus, or viruses?

LEFT: Pancreatic tissue from a diabetic patient; a layer of dead beta-cells (see arrows) surrounds those still producing insulin as T cells move through the tissue. The red stain indicates susceptibility to T cell attack. RIGHT: Normal pancreas; blue stain indicates resistance to T cell attack.

(And what's the point, asks Trucco, "If the kids sneeze for two days, why do you want to vaccinate?") Instead, Trucco wants to localize the super antigen activity in the virus. Then, the biotechnology industry will be able to create a vaccine to protect genetically predisposed children against the super antigen. Kids will still get the sniffles when they are infected with CVB, but they won't get type I diabetes—that is, unless CVB doesn't work alone. Trucco cautions, other viruses may also trigger juvenile diabetes.

But right now, he's focusing on CVB. He wants to pinpoint the segment of its DNA that sets off diabetes. Any day now, he hopes to narrow down the culprit to a few hundred potentially guilty nucleotides.

If it turns out that CVB has a partner, or partners, in its crimes, Trucco may someday track down those viruses as well. For now though, he's keeping it simple—he's focusing on what he knows he can do. ■

FOR MORE INFORMATION:
<http://www.chp.edu>
(See news and events.)

BEYOND INSULIN

With the discovery of insulin in the 1920s, no one dreamed of surpassing insulin injections by transplanting insulin-producing cells. But, according to Massimo Trucco, codirector of the new University of Pittsburgh Diabetes Institute, this may soon be a reality. The institute recently received a grant for close to \$10 million from the Juvenile Diabetes Foundation for seven research projects. One, run by David Fink in neurology, is developing methods for preventing diabetic neuropathy, a widespread problem associated with juvenile diabetes. The other six aim toward a common goal: developing gene therapy techniques for transplanting islet cells, the insulin producing cells of the pancreas, into young diabetic patients.

There are several barriers; but from where Trucco is standing, the path looks clear. The first hurdle: It takes three or four pancreases to supply islets for one transplant. The donor pool simply can't keep up with the demand. So James Pipas, of biological sciences, and codirector of the institute Andrew Stewart, of medicine, are working to grow islets. If they succeed, one donor cell may be expanded for multiple transplants.

Once researchers have the islets in hand, they face the second hurdle: As with any transplant, there is a risk of tissue rejection. If that wasn't obstacle enough, by its very nature, juvenile diabetes attacks islets—even a patient's own cells. So after successful transplantation, researchers must still prevent attacks on the new islets. John Fung, in surgery, and Neal DeLuca and Paul Robbins, in molecular genetics and biochemistry, are all developing methods for transplanting islets without rejection, while Trucco is developing methods for preventing post-transplant immune attacks.

Once these developments are securely under way, these researchers will be well prepared to face their next hurdle: clinical trials.

—RS

NURSE, WRENCH PLEASE

A MACHINE SHOP
THAT SAVES LIVES

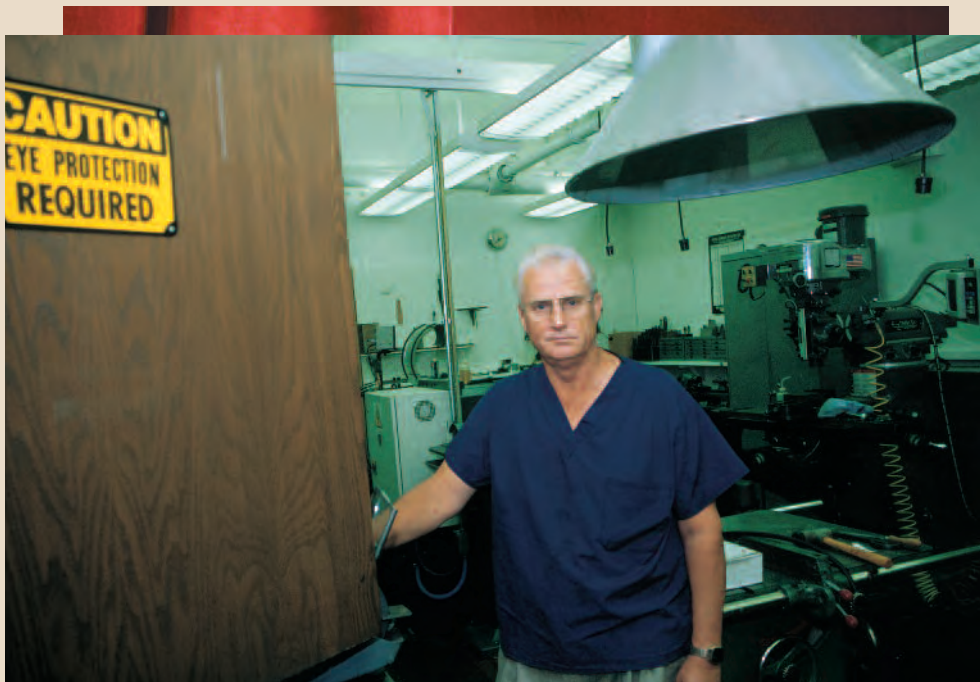
BY MIKE ROSENWALD

It was 5 o'clock, quitting time, and Bill Hughes was getting ready to go home. Then the call came: A patient's mechanical heart wasn't working; it looked like he was about to die.

"I remember the day exactly," says Mark Gartner, a biomedical engineer with UPMC Health System. The part regulating the pump was malfunctioning. Gartner got hold of Hughes who sprinted to the patient's room, took a look at the device, and decided, along with Gartner, that no tool currently in existence could fix the problem.

So Hughes bolted downstairs and built a new wrench—from scratch. Hughes is one of the most resourceful people in the entire Pitt medical community. He is an inventor. And he happens to dream up things that save people's lives, an idea he marvels at regularly by simply saying, "I've got a pretty neat job."

Hughes, who is 52 years old, friendly, with a lot of thin white hair that often creeps in front of his eyes, is the supervisor of the School of Medicine's machine shop. What exactly is a machine shop doing in a medical school? A lot, actually. Hughes, along with his assistant, James MacPherson, is responsible for producing many of the neat gizmos that researchers use at the school. The shop also builds surgical tools and supports, responds to emergencies in the hospital when instruments fail, updates old equipment, and more. Hughes and MacPherson work their magic with about \$200,000 worth of milling machines, welding equipment, and other tools.



Bill Hughes

Here's how the shop typically works (when the two aren't responding to emergencies). The other day a researcher came to Hughes and said she needed a contraption to hold 20 mice as they were being irradiated. The unit had to be designed so that no mouse would be exposed to more radiation than the others. There were no pictures, no designs, only the dimensions of the mice: 3 or 4 inches long, no tail. The machine shop went to work and came up with a round container the size of a small pizza. Inside the container were Plexiglas plates with little bed-like compartments for the mice. Looking at the invention, Hughes said, "You really have to have a good imagination to work here."

In 1965, after graduating from South Vocational Technical High School on Pittsburgh's South Side, Hughes came to work for the medical school. It's the only job he has ever had.

The shop, shared by the Department of Cell Biology and Physiology and the Department of Pharmacology, is rare among medical schools. Researchers and doctors who

consulted with Hughes while they were at Pitt often contact him after they've moved on. As a result, his gizmos are all over the world.

Over the years, the shop has taken on Hughes's personality: fast-working, creative, with an emphasis on organization. (He uses a different cologne each day of the week, with each one labeled by day.) If you are with Hughes, you best have your walking shoes on. Hughes walks like somebody was expecting him 10 minutes ago.

It was that quick step that helped save the man with the faulty heart pump.

Gartner says, "Somewhere that man is hopefully living a happy and healthy life. It's wonderful to have someone like [Hughes] around, someone who can do just about anything."

"Geez, there was something wrong with that pump," Hughes remembers.

"Some screws had popped and this thing was going to pop. I went over and worked on it, right as the patient was lying there. I was pretty scared, but we got things right. To think that he lived, that's pretty neat."

LIGHTS OUT

SURGEONS WORKING

MEDICAL EDUCATION OF A CENTURY PAST | BY REBECCA SKLOOT



COURTESY PARDOE FAMILY

The school's surgical operating theater, c. 1907

In the twilight of the 1800s, Dr. E. A. Wood, an Allegheny County physician, made this observation: "The human system with all its ills is the same to-day as it was a century ago, but if one were curious to know how medical practice has changed, let a

young graduate be started on his way with the old fashioned [doctor's] bags, with their contents."

According to Dr. Wood, "Calomel, the lancet and the blister constituted the armament of the old heroes."

To best capture the changes our twentieth century has seen in medical education, perhaps the place to start is back in the classroom, a classroom Dr. Wood would recognize:

Seven doctors surrounded a patient on an exam table as they lifted and bent his body into position. With thin aprons shielding the fronts of their starched suits from blood, the men leaned in and held the patient steady. A colleague knelt on the floor, his apron protecting his trousers from dirt. With one bare hand he steadied the table, with the other he leaned in with a saber-toothed saw to begin amputating the patient's leg, just below the knee. While the doctors worked with intense concentration, men of all ages leaned forward from their amphitheater tiers. They wore matching black suits with white shirts and ties. Some dangled their hands over the rail surrounding the surgery floor as they craned their necks, leaned on their neighbor, and held spectacles to their eyes for a clear view. Someday soon, they would perform this surgery. They needed to see how it was done.

Outside on the cobblestone streets of Pittsburgh, where even in midday the air was so black with soot that buildings vanished into darkness only feet from the ground, typhoid fever ran wild. The disease killed more per capita in Pittsburgh than anywhere in the world; but the fever was only one of many problems. Factories, steel mills, and a maze of railroads crowded the banks of the city's winding rivers. Workers from around the world squeezed into congested, soiled housing and packed into mills. Pittsburgh became an incubator of injury and disease. Industry, with its mines, railroads, and pollution, was a medical hotbed.

The people demanded health care. So by 1886, after years of struggle, two local hospitals and the Western Pennsylvania Medical College were born. The school had no full-time medical faculty, but doctors from neigh-

boring hospitals and private practices came to share their knowledge as students crammed into amphitheaters, hungry to learn.

The young men craning their necks during the amputation were accustomed to their position. They had chosen their seats on the first day of class. One-by-one they had filed into the room, handed the dean their \$130—the full tuition for their medical education—and picked a seat. Those who came late found themselves high above the amphitheater floor, leaning in for the full view. From similar seats around the school, these students watched surgeries of all kinds, saw doctors examine patients and dissect cadavers. However if a student examined a patient first-hand, he was one of a fortunate minority.

Most of the students didn't have college degrees. There's a chance they never graduated from high school. Before paying their fee and choosing their amphitheater seats, they were tested in math and reading skills, but if they didn't pass, they were admitted *on condition*. Schools around the country would not require college degrees and solid entrance exam scores until the 1910s. And in Pittsburgh, the Medical College administration was particularly wary of such "reforms." Personality, they argued, not intelligence alone, should be a requirement for admission. Grades could predict a student's ability to learn a subject, but they said nothing of how the student would be as a physician. Grades and

LIBERTY BRIDGE AND THE MCCARDLE ROADWAY, DOUGLAS COOPER



TYPHOID FEVER.

This Notice is Posted in Compliance with Law

—Every person who shall wilfully tear down, remove or deface any notice posted in compliance with law, shall be fined not more than seven dollars.—GENERAL STATUTES OF CONNECTICUT, REVISION OF 1902, SECTION 1173.

Town Health Officer.

NATIONAL LIBRARY OF MEDICINE

top: Artist Douglas Cooper represents an evolving Pittsburgh

above: Typhoid fever killed more per capita in Pittsburgh than anywhere else

below: A mule-drawn ambulance



WEST PENN HOSPITAL

One-by-one they had filed into the room and handed the dean their \$130—the full tuition for their medical education.

test scores didn't measure compassion, creativity, and dedication.

As years went on, the school would face a daunting question: How does an admission board judge personal quality? They eventually agreed on an answer: Create a system that combines academic evaluations with intuition about students as individuals.

At the turn of the twentieth century, life expectancy was less than 50 years. Suffering and premature death were a part of everyday life, but things were starting to look up. There was a new technology, one that took pictures through the skin, allowing physicians to see inside the human body. Pasteur had demonstrated the role microorganisms play in disease and Lister had developed antiseptic theories that promised to shed light on the bacterial problems that killed millions. Suddenly, the baffling world of illness was looking a bit more intelligible. But in day-to-day practice, there was little a physician could do for his patients. The most effective therapeutics in a doctor's bag were aspirin, heroin, and cocaine—substances that relieved pain but had no effect on the underlying cause of disease.

In 1901, the Pan-American Exposition in Buffalo came to an abrupt halt with a gunshot whose wrath symbolized the limitations physicians faced. Gunfire cracked through the air, and President McKinley fell wounded, a bullet lodged in his abdomen. He was rushed to the infirmary. As physicians opened his abdomen they wore no caps or gowns. They operated without lights. Ether, the only anesthetic option, was flammable—lantern flames would ignite the air. So as the sun descended and night approached, doctors used mirrors to guide the dimming light into the room. For over an hour, physicians dug through the president's body with their bare hands, in search of a bullet they would never find.

As anxious crowds huddled outside, doctors fought to sustain the president with raw-egg enemas and injections of strychnine. But after eight days, President McKinley died of gangrene.

The arena for educating students about surgery has moved from open-air amphitheaters to modernized surgical observation suites. Gangrene is no longer the most common outcome of surgery. And as the twenty-first century progresses, medical education will likely see ideas and advances that make last week feel 100 years away. ■



NATIONAL LIBRARY OF MEDICINE

ABOVE: A typical lesson in patient examination, circa 1900



SINCE TIME IMMEMORIAL

For decades, perhaps centuries, perhaps millennia—let's just say, since the dawn of education, students have agonized over how they'll be evaluated by their teachers.

Likewise, students have forever looked for opportunities—a class skit, a cartoon in a student paper, whatever—to turn the tables. In a forgotten corner, *Pitt Med* came across the Class of 1907's yearbook. Sure enough, the students took advantage of the opportunity for some ribbing. Here are some of their reviews of professors:

John Edwin Rigg, MD, Professor of Obstetrics

"Dr. Rigg. . . teaches us by telling some of his own experiences, but if he ever loses that index finger on his right hand, which is constantly shaking to impress facts, we think he will not be able to teach anymore."

William H. Ingram, MD, MS, Professor of Histology, Pathology and Bacteriology

"We challenge any one to produce a man who can talk as much and say as little as Dr. Ingram. However he is an interesting speaker and if you get a chance get him to tell you of some of his experiences. Let us warn you, though, do not get him started on pathology."

James Witherspoon, AM, MD, Professor of Descriptive Anatomy

"His classes are all conducted very quietly, due, no doubt, to the fact that they are always quizzes. About once a year he says a few words not relating to the subject of anatomy."

Herman W. Heckelman, MD, Professor of Diseases of the Eye and Ear

"Dr. Heckelman is a well built man with a commanding appearance and a nice white beard, which the boys say resembles the Bundle of His."



CLOCKWISE FROM LEFT: Drs. Rigg, Ingram, Witherspoon, and Heckelman

PORTRAITS: THE OWL, 1907

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



lished a humanitarian award for med students at Pitt, encouraging future doctors to see how reaching out can enrich their lives and the lives of others.

Scott recalls a moment during a recent Montserrat visit when she dropped in on a former patient. The woman, a 92-year-old retired school teacher, was living in a church-turned-shelter in 1997 when Scott's team removed one of the cataracts

that blinded her. When Scott visited her last, the woman walked onto a porch, looked at Scott and said, "I always appreciated when someone read the Bible to me, but there's nothing like my being able to read it myself." Moments like these, Scott says, serve as reminders of how valuable a few volunteer hours can be.

Miles from that porch in the Caribbean, tucked in the woods of Ligonier, Scott's phone rings again. A friend is calling. It's time to put together another team of volunteers and head back to Montserrat. ■



Montserrat's volcano

DOROTHY CHRISTIE SCOTT'S VISION

AN OPHTHALMOLOGIST REACHES OUT

BY STEPHANIE NELSON

The phone rings often for Dorothy Christie Scott (MD '56). People call asking for her opinion, for her advice. And whether she's in her Ligonier, Pennsylvania, home or on a remote island, she is always the first to offer help.

Scott is no stranger to "firsts." She was one of the first surgeons in Pittsburgh to implant intraocular lenses after cataract removal and was the first female president of Pitt's Medical Alumni Association, the Pennsylvania Academy of Ophthalmology, and St. Francis Medical Center's staff.

Scott devoted more than 30 years to teaching, but her contributions go beyond associations and classrooms. Scott leads teams of ophthalmologists to the tiny Caribbean island of Montserrat, where they provide free eye care. The island, a second home to Scott, was not always in dire need. But in 1997, Montserrat's volcano erupted, and everything changed. Thousands were displaced and many relocated to other islands, fragmenting the once close-knit community. Scott admires those who stayed to rebuild—she wants to help them any way she can.

The year of the Montserrat volcano, Scott devoted more than time and effort: she estab-

on the stairs, rolled down the steps, and landed flat on his back—right in the room where the patient was waiting. The ER nurse, taken aback, spluttered, "The doctor is here!"

It's hard to tell what's hyperbole in old medical tales, but if you are listening to Sam Tisherman, you don't really care. He has great stories to tell. Many of those fantastic memories are simply products of the extraordinary times of which he was part and the extraordinary people with whom he worked. In recognition of the outstanding education he received, last year Tisherman endowed a lectureship in medical ethics, the first of which was held in December. It featured noted ethicist George Annas of Boston University.

Tisherman worked with the best of the best. In 1950, before even enrolling in medical school, he served alongside Jonas Salk, as an assistant virologist. Tisherman interned under the world-renowned T. S. Danowski. And at Presbyterian, he was one of Jack Myers's first interns. Those were rocky days. As the now legendary Myers built his house staff, many residents and interns didn't last long. "One day Myers came up to me and said, 'Tisherman, yesterday you were an intern, today you are a resident.' It wasn't that I was so good, I was the only one left!" says Tisherman.

His studies under the likes of Myers served him well. Tisherman went on to contribute important long-term research findings on familial pheochromocytoma. He also founded an internal medicine practice and has been recognized by the American College of Physicians. And as a clinical associate professor of medicine, he trained many talented internists himself.

The school has become part of a Tisherman family tradition: Tisherman's son Samuel A. Tisherman (MD '85) and daughter-in-law Susan Dunmire (MD '85) are both on the faculty at Pitt and active in the Medical Alumni Association.

Tisherman, who was born in Oakland, attended Frick School and received both his BS and MD at Pitt. He likes to say his future was always a block ahead of him.

And what a future that has been. ■



Tisherman

ONE BLOCK AHEAD

A LECTURESHIP PAYS TRIBUTE TO SAMUEL E. TISHERMAN

BY ERICA LLOYD

It's hard enough to get some rest if you're a resident in a major urban hospital. If you talk with Samuel E. Tisherman (MD '55) he'll tell you that decades ago, when he was on a rotating residency at Magee-Womens Hospital, not only was he on emergency call throughout the night, he had to live right above the boiler room.

"I was so tired," he says.

One particularly hard night, Tisherman was awakened to respond to a call in the ER. As he rushed to the patient, he lost his footing



CLASS NOTES

'50s

FELIX "BEBE" MILLER, MD '55, retired from private practice in obstetrics and gynecology and is currently director-at-large of the University of Pittsburgh's alumni association board. He is a tireless advocate of the medical school and a senior mentor.

ALVIN MARKOVITZ, MD '58, associate clinical professor of medicine at the University of Southern California School of Medicine in Los Angeles, has been elected to the office of treasurer of the American Academy of Disability Evaluating Physicians (AADEP). AADEP is an international physicians' society, which specializes in occupational, environmental, and disability medicine. Prior to his recent position, Markovitz was chairman of AADEP. In addition to his new appointment, Markovitz recently published a position paper in the journal *Disability* on impairment and disability issues involved in fibromyalgia.

ULTON G. HODGIN JR., MD '59, has announced his retirement after 34 years of private practice. Hodgin, who is retiring from a five-physician infectious diseases and internal medicine group in Albuquerque, New Mexico, says, "Medicine will be replaced with fishing, travel, sports, and restoration of autonomy." During his career, Hodgin's appointments included clinical professor of medicine, president of the New Mexico Medical Society, fellow of the American College of Physicians, and fellow of the Infectious Diseases Society of America. He has been the recipient of the Alpha Omega Alpha faculty award from the University of New Mexico, the Distinguished Internist Laureate Award from the New Mexico chapter of the American College of Physicians, and the honor of Mastership from the American College of Physicians.



The Owl, 1950

KEITH SMITH, MD '59, spent more than 20 years on the faculty of the University of Texas-Houston Medical School in the Department of Reproductive Medicine. He is now a practicing endocrinologist in Houston, Texas, where he is, as he says, "enjoying practice and fighting managed care."

'60s

FREDERICK BROWN, MD '61, retired from practice last spring after a 32-year career at the Geisinger Medical Center in Danville, Pennsylvania, where he served most recently as the director emeritus of nephrology. Brown is hailed as a pioneer in the science of dialysis; rumor has it, he once turned an old washing machine into a home dialysis unit.

JAMES R. SMOLKO, MD '61, has retired from practice after an extensive career in anesthesiology. Most recently, he served as chairman of the Department of Anesthesiology at York Hospital in York, Pennsylvania, in addition to holding appointments as president and CEO of the Anesthesia Association of York, president of the York County Medical Society and York Hospital Medical Staff, and delegate to the Pennsylvania Medical Society.

BARRY M. BRENNER, MD '62, was the recipient of the 1999 Jean Hamburger Award for his pioneering work in nephrology. Brenner, now Samuel A. Levine Professor of Medicine and director of the renal division at Harvard's Brigham and Women's Hospital, carried out classic studies that led to formulation of the

well-known "glomerular hypertension theory," otherwise known as "Brenner's Theory." Brenner completed his residency at the Bronx Municipal Hospital Center in New York, where he served as chief resident in medicine; he was granted a postdoctoral fellowship at NIH. He was chairman of the American Association



The Owl, 1972

for the Advancement of Science's medical sciences section, president of the American Society of Nephrology, and president of the American Society of Hypertension. He is the author of several essential textbooks, including *The Kidney*, *Hypertension*, *Renal Pathology*, and *Acute Renal Failure*. Brenner has received numerous honorary degrees and awards, including Pitt's Hensch Award and the Homer W. Smith Award, given by the New York Heart Association and the American Society of Nephrology as the highest award for scientific achievement in renal physiology.

JAMES RUSSELL

HUTCHISON, MD '62, is vice-president of medical staff affairs at Presbyterian Healthcare Services in Albuquerque, New Mexico, where he was medical director of the Women's Program and the Department of Obstetrics and Gynecology. He also served as chair of the Committee on Professional Liability for the American College of

Obstetricians and Gynecologists.

JOHN R. KRAUSE, MD '66, was appointed chairman of pathology and laboratory medicine at Tulane University Medical Center in New Orleans in July. Krause previously served as professor of pathology, vice-chairman of pathology, and director of laboratories at Tulane. Before going to Tulane, Krause completed a pathology residency at UPMC and spent the following 20 years at Pitt where he was professor of pathology and vice-chairman of graduate medical education for the Department of Pathology.

RONALD RABINOWITZ, MD '68, was selected as a contributor for *The Merck Manual's* Centennial Edition. Rabinowitz contributed and reviewed sections on renal and genitourinary defects. The manual is considered the most widely used medical textbook and is the longest continually published medical reference.

'70s

NEIL A. HALPERN, MD '72, is now the chief of critical care medicine in the Department of Anesthesiology and Critical Care Medicine at Memorial Sloan Kettering Cancer Center in New York, New York. For 14 years prior to his recent appointment, Halpern served as director of the Surgical Intensive Care Unit and Stat Lab at the Veteran's medical center in Bronx, New York.

RICHARD KASDAN, MD '72, organized the first outpatient magnetic resonance imaging facility in Pittsburgh in 1985. He is now medical director of four

REUNIONS

of these facilities in the Pittsburgh area, as well as chairman of the Department of Neurology at Jefferson Hospital in Pittsburgh and clinical associate professor of neurology at Pitt. He is board certified by the American Board of Psychiatry and Neurology and a member of the American Society of Neuroimaging.

ERNEST E. MOORE, MD '72, received the Robert Danis Prize from the International Society of Surgery.

DAVID L. STEED, MD '73, has been chosen president-elect of the Wound Healing Society. Steed, now a professor of surgery at Pitt, has held numerous faculty positions with the University and UPMC Health System. He has led research studies to promote healing of diabetic foot ulcers and to test the effectiveness of human-derived growth factors. Steed is director of the Wound Healing and Limb Preservation Clinic at Falk Clinic.

SANDRA M. SCHNEIDER, MD '75, was elected president of the Society for Academic Emergency Medicine, the primary national society for university emergency medicine physicians. In addition to her recent appointment, Schneider is professor and chair of the Department of Emergency Medicine at the University of Rochester in Rochester, New York.

CAROL CONGEDO, MD '76, retired from practice due to disability. Congedo, who was diagnosed with systemic lupus erythematosus (SLE), is now chairman of the Patient Services and Outreach Committee of the Southwestern Pennsylvania chapter of the Lupus Foundation of America (LFA). She is also a member of the *National Lupus News* Editorial Board and the LFA's Patient Educational Materials Review Committee. She is the author of *Prednisone User's Exercise Manual* and *Lupus in the Workplace*.

JEFFREY MILSOM, MD '79, has been appointed professor of surgery and chief of the Division of Colorectal Surgery at the Mount Sinai School of Medicine; he is also an attending surgeon at Mount Sinai Hospital where he serves as codirector of the new Minimally Invasive Surgery Center. Milsom developed minimally invasive laparoscopic colorectal surgery techniques. His work has resulted in numerous journal and book publications, including coauthoring the first book on laparoscopic colorectal surgery.

'80s

WILLIAM A. PETIT JR., MD '82, was recently voted teacher of the year by the Primary Care Internal Medicine Residency Program at the

University of Connecticut Health Sciences Center. Petit is director of the section of Endocrinology, Metabolism, and Diabetes, and medical director of the Joslin Center for Diabetes at New Britain General Hospital in New Britain, Connecticut.

KENNETH J. DZIALOWSKI, MD '84, serves on the UPMC Health System's Committee for Women's Health. He is chairman of the obstetrics and gynecology department at Jeannette District Memorial Hospital in Jeannette, Pennsylvania, and serves on the Medical Executive Committee.

SHARON L. HRABOVSKY, MD '89, now assistant professor of dermatology at Pitt, specializes in mohs micrographic surgery—a specialized skin cancer technique. Hrabovsky joined the Pitt faculty in February of 1998 after finishing a fellowship at Ohio State University and an extended residency at Case Western Reserve University. She began her residency in ENT, but after receiving a grant from NIH and moving into the laboratory to study basal cell carcinomas, she switched to a dermatology residency. She has since published papers on photodynamic therapies for skin cancer and immunofluorescent studies of basal cell carcinoma. Hrabovsky organized her class's 10th reunion, and would like to start a music therapy program for cancer patients. She has been in contact with the Pittsburgh Symphony Orchestra and is looking for volunteers to help with the program. For more information: hrabovskysl@msx.upmc.edu

'90s

JOHN C. CALDWELL, MD '90, is an assistant professor at Pitt in anesthesiology and critical care medicine and staff cardiac anesthesiologist at UPMC Presbyterian in Pittsburgh. Caldwell was involved in developing the integrated coronary revascularization technique for cardiac surgery. The technique, which combines heart bypass surgery and angioplasty, is a minimally invasive procedure that can be completed within two hours.

KAREN L. BRADY VELAZQUEZ, MD '96, completed her residency at Western Pennsylvania Hospital in family practice and accepted a faculty position at the UPMC Shadyside Family Practice Residency Program. She now sees patients at the East End Community Health Center. —RS

Pitt Med is eager to publish news of its fellow and resident alumni as well! See attached form.



The Owl, 1929

CAMEO APPEARANCE

Between September 25th and 27th, the **CLASS OF '59** swapped stories and sipped iced tea at Virginia's Martha Washington Inn. But **ROBERT HORSCH, KEITH SMITH, AND NANCY SWENSEN**—reunion organizers—also kept their classmates busy. They toured the town of Abingdon, hiked the Virginia Creeper Trail, attended a formal banquet, and witnessed the *pièce de résistance*. . . . At the historic Barter Theatre, the class gathered for a rendition of *Blackbirds of Broadway*. As the performance was about to begin, an actor walked on stage ringing a bell, wearing a white coat; he introduced himself as **DR. HOOKER**, returned from the grave with a message for the class. Hooker had written a letter in their final yearbook, a challenge to do something important with their careers. Now he was back with a similar message, but this time, he challenged them to make the most of their retirement.

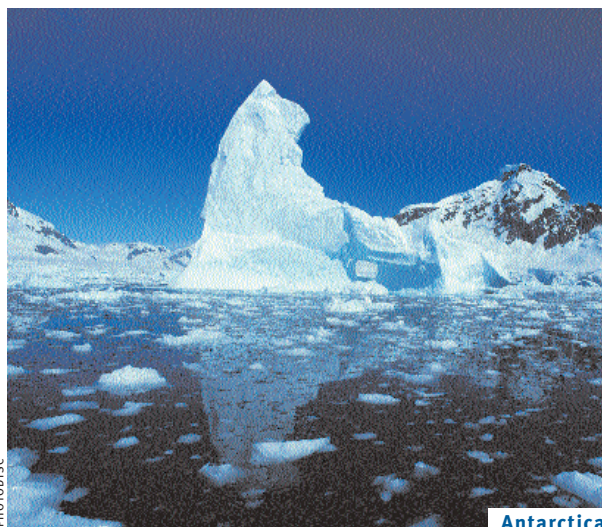
THE CLASSES OF '64 AND '74

both celebrated reunions on November 6. The Class of '64 got together for their 35th at the Pittsburgh Athletic Association. And down the street, at the University Club, the Class of '74 caught up and shared memories.

THE CLASS OF '89 cheered from more than two dozen seats at the Pitt-Notre Dame game—the last game to be played in the old Pitt Stadium. **SHARON L. HRABOVSKY**, MD '89, organized the 10th reunion, which included a tailgate party.



Members of the Class of '44 at their reunion in October



PHOTODISC

Antarctica

IN MEMORIAM

FRANCIS J. ARCH JR. (MD '52), DECEMBER 5, 1998

RICHARD J. BENDER (MD '64), JUNE 20, 1999

JACK C. W. BROOKS (MD '59), OCTOBER 31, 1998

J. VAN S. DONALDSON (MD '44), MAY 16, 1999

HENRY W. FRALEY (MD '37), JUNE 24, 1999

HARRY L. GALANTY (MD '89), JULY 27, 1999

HARRY L. GERSTBREIN (MD '56), SEPTEMBER 22, 1999

ELLSWORTH B. HARRIS (MD '47), SEPTEMBER 19, 1999

ROBERT G. HEATH (MD '38), SEPTEMBER 21, 1999

JEROME KLEINERMAN (MD '46), AUGUST 6, 1999

JOHN LOUIS KOSTYAL (MD '40), AUGUST 10, 1999

HARRISON H. RICHARDSON (MD '45), JULY 17, 1999

THOMAS L. ULICNY (MD '73), JULY 31, 1999

STEPHEN D. WARD (MD '54), OCTOBER 7, 1999

THEODORE R. WHITAKER (MD '41), JULY 13, 1999

HARRISON H. RICHARDSON, MD '45

JUNE 16, 1919—JULY 17, 1999

Amidst an archipelago of mountains covered and bound together by ice, the peak of Antarctica's Mount Richardson reaches toward the sky. Its namesake, Harrison Holt Richardson (MD '45), the youngest member of the 1939-41 Antarctic expedition led by Richard Byrd, launched his adulthood behind a team of howling sled dogs pulling him 850 miles inland on the continent of ice. After capturing the first-ever color film images of the region, Richardson returned home to Pennsylvania to enroll in the University of Pittsburgh's medical school.

But Richardson's adventures were far from over. After completing medical school, he devoted years of service as a medical officer for Navy expeditions to Antarctica and the Arctic before settling down in his hometown of Beaver, Pennsylvania. He practiced radiology for 30 years at both the Beaver Valley General Hospital and the Rochester General Hospital, where he served as chief radiologist. Richardson, after a lifetime of trekking across the globe, died in his son's home of complications from hip surgery.

—RS

ROBERT G. HEATH, MD '38

MAY 9, 1915—SEPTEMBER 21, 1999

In the summer of 1936, Robert Heath, MD '38, packed into a car with buddies from the University of Pittsburgh School of Medicine. They had decided to spend the next couple of months driving across the country and back—and this was well before the interstate highway system was built. The young men were eager to see new places; they relished the thought of the discoveries awaiting them.

Heath would continue that journey of discovery throughout his life. He earned national and international acclaim for his research and teaching in the fields of psychiatry and neurology. Through the years, the Pitt med grad was distinguished with many honors, including the Gold Medal Award of the Society of Biological Psychiatry.

At the core of Heath's extensive studies was a desire to find more effective ways to treat patients, particularly those suffering from severe chronic behavioral disorders. And that he did. He is regarded as a modern pioneer in the study of schizophrenia as a biologically caused disorder, and his innovative studies of behavior and the brain led to further investigation into the causes of mental illness and dramatic changes in methods of treatment.

As the founding chairman of Tulane University's Department of Psychiatry and Neurology, a position he held for 31 years, Heath directed the training of more than 400 residents. Tulane acknowledged his achievements by establishing a University Chair and an endowed lectureship in his name.

To this day, Heath's spirit of discovery continues to inspire many. —JE

MEDICAL ALUMNI ASSOCIATION OFFICERS

PHILLIP BALK, MD '59, President
 SUSAN DUNMIRE, MD '85, President-elect
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PHILLIP BALK: THE PRESIDENT OF THE MAA THINKS HE HAS A LOT TO LEARN, AND HE'S GLAD.

BY THOMAS MITCHELL



Phillip Balk

Did you know,” asks Phillip Balk (MD ’59) with a raised eyebrow, “that there is no Japanese term for hot flash?” He had no idea until his daughter told him one night over dinner. Balk, a visiting professor of clinical medicine at Pitt, is used to this kind of dinner-table discussion. Between Balk and his three physician children, there’s a lot of teaching going on around the house. At first, Balk thought it seemed odd that the Japanese didn’t talk about hot flashes. But Japanese women don’t experience menopause like Western women do, his daughter explained. They don’t have the flashes or the sweats. Their diet, unlike ours, is full of estrogen-like compounds that ease the transition into menopause. “It’s fascinating,” Balk says. “It really is.” And for him, anything that fascinates is worth learning now, and teaching later. The catch is, it’s hard to find anything that *doesn’t* fascinate him. Whether it’s at the dinner table, or in the hospital, Balk loves to learn. And he loves to teach.

At UPMC Shadyside, where he is involved with the Internal Medicine Residency

Program, Balk navigates the halls with alert eyes, happy to chat with anyone he runs into. It could be one of the many residents he teaches, or his old anatomy professor, who is now a colleague. Just like dinnertime at home, he sparks an educational give-and-take.

According to Balk, one of the most important aspects of medicine is the approach. So

For him, anything that fascinates is worth learning now, and teaching later. The catch is, it’s hard to find anything that *doesn’t* fascinate him.

that’s what he teaches. He instructs residents on how to approach a patient: what tone of voice to use, how to examine and relay what one has found. Sure, techniques can be explained in a classroom, but, in Balk’s eyes, only years of clinical experience earn a doctor these talents. And after 30 years in private practice as a rheumatologist, when he advises residents, it’s with experience from decades of learning by doing.

Today, he is in the position to help undergraduate med students as well: In addition to practicing medicine and working with residents, he decided to take on the duties of Medical Alumni Association (MAA) president.

Leaning slightly forward in his chair, Balk shakes his head and says, “You know, the cost of school has just zoomed.” Today, on average, indebted Pitt medical students graduate owing almost \$104,000. This bothers him. Through his position with the MAA, Balk wants to do something about it. He aims to continue fostering education with loans, scholarships, and grants for students.

“I think that’s [the MAA’s] biggest role now,” says Balk.

But there’s more. And he takes particular delight in describing the little things.

The alumni can’t help students in their rotations, but through the MAA, they can supply the white coats. And more importantly to Balk, they can make sure every student has a pager so, unlike generations of alumni before them, today’s students won’t miss out when they are out of arm’s reach. In his days at Pitt, communication was sometimes a problem. Especially when it came to observing autopsies. The morgue would try to call students, leaving messages around school saying, *Something came in, come quick*. But it was easy to miss the call.

When Balk reflects on his time as a medical student at Pitt, he says, “There simply wasn’t enough time in the day.”

After 40 years in medicine, Balk has a lot to teach.

But he also has his students, colleagues, and children from whom he continues to learn.

And he thinks that’s great. ■

Time out to look back

Speaking of millennia, herbal charts like these were common physician tools for most of the past one-thousand years. (Valentini, Michael Bernhard, circa 1700, *Plants of Medicinal Value to Particular Human Body Parts*.)