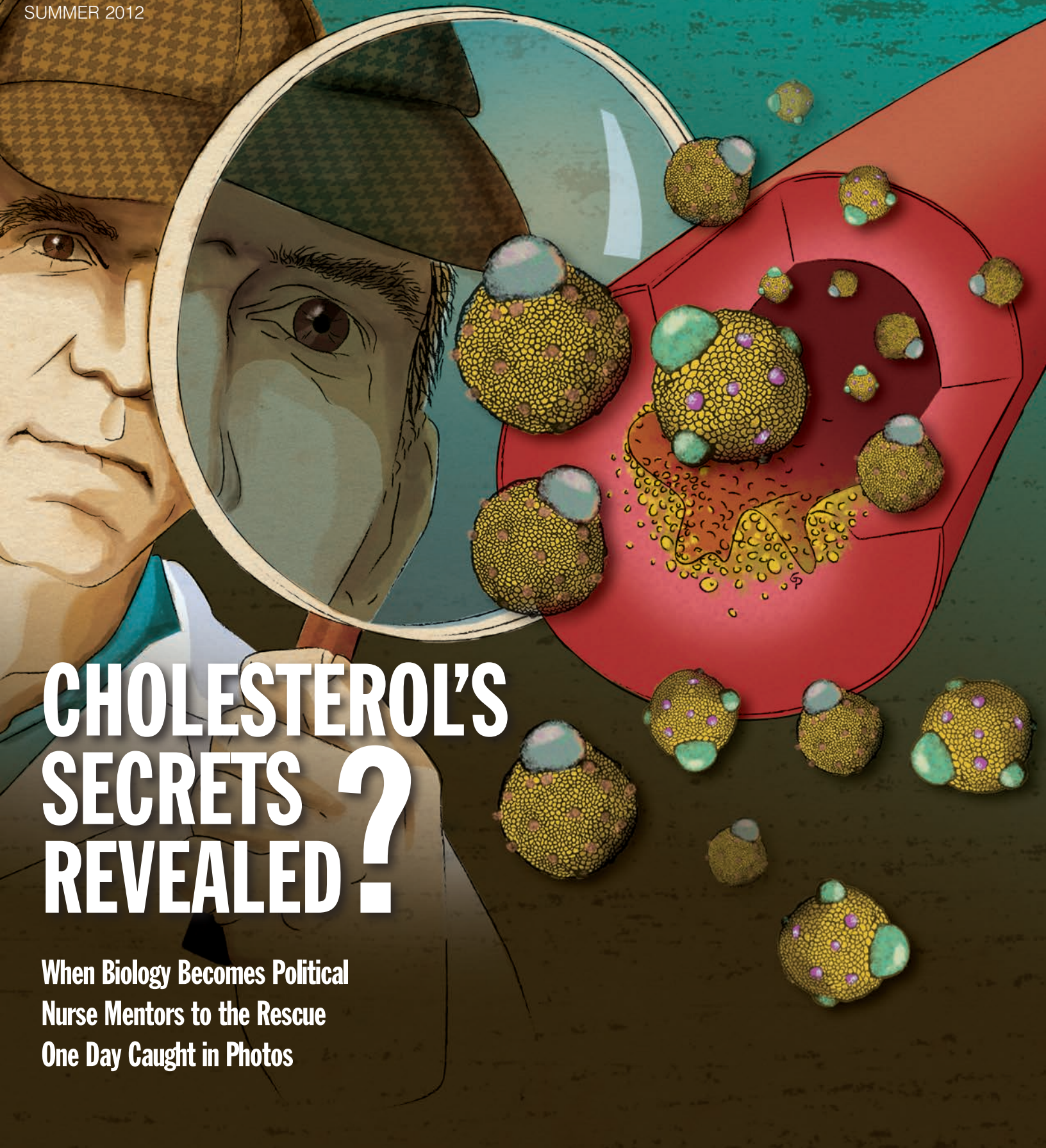
# PENN Medicine

SUMMER 2012



# CHOLESTEROL'S SECRETS REVEALED?

When Biology Becomes Political

Nurse Mentors to the Rescue

One Day Caught in Photos

## Seeking Collaborations

All scientists dream of making a discovery that will change their fields forever, adding a building block to the knowledge base that others will use to advance science even further. Some of these discoveries also have the potential to improve health, by uncovering the cause of a disease or by discovering a new drug. However, the path from discovery to clinical application is circuitous and long, and frequently there are potholes if not dead ends. At Penn Medicine, we are deeply committed to "translational medicine," a theme that focuses on strategies to compress the time from discovery to application in clinical practice. Success in translational medicine requires brilliant scientists, a culture that fosters innovation and teamwork, and a substantial infrastructure ranging from core facilities and information technology to research administration. In this column, I want to underscore the importance of effective tech transfer and partnerships with industry, if we are to maximize the goal of translating research for the benefit of patients.

A few decades ago, collaborations between industry and academic medicine were uncommon because the cultures and approaches to R&D were very different. An inflection point occurred when Herb Boyer and Stanley Cohen, M.D. '60, teamed up to create recombinant plasmid DNA. Boyer studied enzymes that created DNA with "sticky ends" while Cohen had identified antibiotic resistance genes on plasmids. Meeting in a coffee shop, they plotted an experimental approach that is now used routinely to cut and paste foreign DNA into designer plasmids to create recombinant DNA. Genentech was launched and the biotech industry soon flourished, producing unlimited amounts of recombinant insulin and many other valuable drugs.

Another inflection point was the passage of the Bayh-Dole Act in 1980. This act gave universities ownership of their intellectual property, thus creating an incentive to license discoveries to industry yet with enough protection to encourage further development. However, successful academic-industry relationships have developed gradually and not without challenges. At a national conference hosted by the University of Pennsylvania in 1982, A. Bartlett Giamatti, then president of Yale University, underscored the cultural differences. The academic imperative is "to seek knowledge objectively and to share it openly and freely." On the other hand, Giamatti continued, the industrial imperative is "to garner a profit, which frequently creates the incentive to treat knowledge as private property." In addition to these cultural and strategic differences, the potential for conflicts of interests has garnered attention, leading to greater transparency and clearer guidelines from NIH, institutions, and professional organizations.

Despite these challenges, the symbiotic relationship shared by academia and industry is powerful. With billions of dollars each year in federal funding, academic medical centers are ripe with discoveries poised for translation; industry holds complementary expertise in device and drug development, as well as the financial resources to support expensive but essential clinical trials. As a recent report from the Tufts Center for the Study of Drug Development stated, pharmaceutical firms are taking aggressive steps "to offset ever more costly and risky drug development" and are expanding partnerships with universities and academic medical centers "to better identify potential breakthrough therapies based on advances in basic research and to guide external early-stage research."

At Penn Medicine, we have established multiple corporate partnerships, such as sizable unrestricted grants from GlaxoSmithKline, Pfizer, and AstraZeneca, as well as many other examples of sponsored research and licensing agreements. Several of our faculty members have been fortunate to launch start-up companies with industry. The cover story in this issue explains how Dr. Daniel Rader, professor of medicine, received the rights to a drug developed by Bristol-Myers Squibb and used it to treat patients with homozygous familial hypercholesterolemia, which causes high LDL cholesterol. Based on the success of these studies, Penn subsequently re-licensed this drug to Aegerion. This is an important example of the distinctive capacity of academic medicine to advance treatment of so-called orphan diseases.

In the future, we hope to see more examples like this at Penn Medicine. For a biomedical research enterprise of our scale and quality, historically we have not achieved the level of tech transfer one might expect. This was part of the rationale to create the new Institute for Translational Medicine and Therapeutics (ITMAT) along with a series of disease-oriented centers and institutes. ITMAT helped catalyze a successful application for the prestigious Clinical and Translational Science Award grant from the NIH. In 2011 we launched a Center for Orphan Disease and Treatment (*Penn Medicine*, Fall 2011), which will focus on novel therapeutic approaches for diseases that while individually rare, together affect more than 25 million Americans. We also launched the Basser Research Center (see p. 2), which will have a sharp focus on developing new therapies for women with mutations in the BRCA 1 and 2 genes that predispose to breast and ovarian cancer. As part of our strategic planning process over the last year, great emphasis emerged on the need to build on our success by further enhancing tech transfer and partnerships with industry, and by developing an academic culture deeply committed to ensuring that discoveries provide greater value to society.

In today's environment, in which funding agencies and donors are increasing their emphasis on research that can more quickly benefit patients, areas of "translational medicine" are gaining in importance. On the Penn Medicine campus in May 2011, Dr. Francis Collins, director of NIH, explained why NIH was creating the National Center for Advancing Translational Sciences: its mission involves catalyzing the development and testing of novel diagnostics and therapeutics across a wide range of human diseases and conditions. Consistent with this NIH goal, Penn Medicine established a master's program in translational research. Graduates of the program will be able to apply contemporary research tools to clinically relevant areas of investigation and will be competitive in seeking research support.

ITMAT also offers the Commercialization and Entrepreneurship Program. In April, for example, one of the speakers was Steven J. Siegel, M.D., Ph.D., associate professor of psychiatry and director of the translational neuroscience program. He described his path to commercializing his research to produce a long-term system of delivering antipsychotic medications to patients. His research helped launch a start-up company with NuPathe, a biopharmaceutical company in the Philadelphia area. The ITMAT program may inspire other members of our faculty to think along similar entrepreneurial lines.

In these very challenging times for academic medical centers, we must seize the opportunity for increased collaboration with corporate partners that share our interests. We have much to offer, including the integration of our research and clinical facilities and, most importantly, our shared ethos of rapidly advancing new therapies and cures. Combining our intellectual resources with the power of industry will have a tremendous impact on the practice of medicine, our health system, and our patients. ●

J. Larry Jameson, M.D., Ph.D.
*Executive Vice President of the University of Pennsylvania for the Health System*
*Dean, Perelman School of Medicine*

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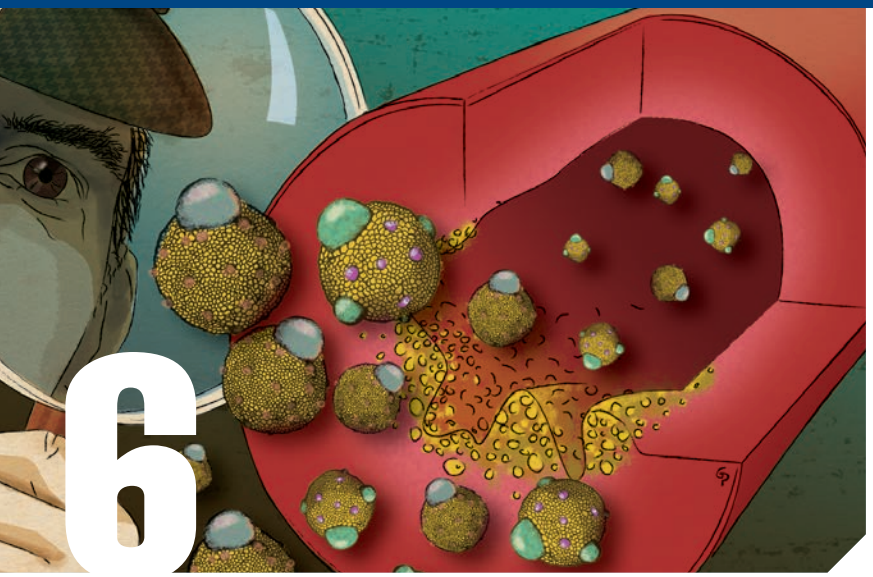

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## INVESTIGATING THE MYSTERIES OF CHOLESTEROL

*By Marshall A. Ledger*

**One of Daniel Rader's grants was the "Distinguished Clinical Investigator Award," from the Doris Duke Charitable Foundation. In his career, he has continued to live up to that title, becoming one of the leading experts on cholesterol metabolism. According to Richard P. Shannon, M.D., chair of the Department of Medicine, Rader is "the foremost figure in the translational approach to HDL as a therapeutic target."**

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## THOSE FIRST FRIGHTENING DAYS IN CLINICAL ROTATION

*By Sally Sapega*

**Many medical students still remember how they felt when beginning their first clinical rotations. Often they had no idea of the various roles of the nurses, and the nurses didn't know how much the students knew. A new nurse mentor program, perhaps the only one of its kind in the nation, helps the students learn the ins and outs of the units and where to go for answers.**

## Departments



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## A MATTER OF HEART

*By Nefertari Nelson-Williams*

**Nine months pregnant, the author was resting at home when it suddenly felt "like a piano or an elephant was sitting on my chest." When she was flown by helicopter to HUP, she learned that one of her coronary arteries had broken in half. HUP's doctors and nurses worked to save the mother – and her baby.**

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## A DAY CAPTURED IN PHOTOGRAPHS

*By Daniel Burke*

**As part of a university-wide initiative, Daniel Burke turned his camera on many different sites and many different people on April 14. Along the way, he captured nurses arriving for work in the early morning, an ER team conferring, a technician monitoring sleep studies, medical students studying, and surgeons operating, all part of a typical day in the life of Penn Medicine.**

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## IN THE THICK OF THINGS: JONATHAN MORENO

*By John Shea*

**In his most recent book, Jonathan Moreno, Ph.D., ranges across disciplines to examine America's longstanding ambivalence toward science. *The Body Politic* shows how biology has become part of national politics – in short, *biopolitics*. After writing books on secret state experiments on humans and on neuroscience and national defense, Moreno shows no sign of leaving contentious topics behind.**

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## Gift Establishes Center for Inherited Cancers

Thanks to a $25 million gift from alumni Mindy and Jon Gray, the University of Pennsylvania will establish the Basser Research Center to support research on the BRCA1 and BRCA2 genes. The harmful forms of such genes are linked to greatly increased risks of developing breast and ovarian cancer. The center is named in honor of Mindy Gray's sister, Faith Basser, who died of ovarian cancer at age 44.

According to Amy Gutmann, Ph.D., president of the University, "In creating this first-of-its-kind center, the Grays' gift endows Penn researchers and clinicians with the crucial resources required to identify innovative ways to prevent and treat inherited diseases."

"We hope that the Basser Research Center will eliminate BRCA-related cancers and, in doing so, provide a road map for curing other genetic diseases," said Mindy and Jon Gray.

The center will be located within Penn's Abramson Cancer Center. The gift will

create the endowed Basser Professorship, recruit additional faculty, enhance core technologies such as bioinformatics and DNA vaccine production, launch an annual lectureship, and establish the Basser Prize to honor cutting-edge research. The gift will also support research with a particular focus on interdisciplinary work and an acceleration of bench-to-bedside implementation of scientific findings.

Susan Domchek, M.D., associate professor of hematology/oncology and current director of the MacDonald Women's Cancer Risk Evaluation Center in the Abramson Cancer Center, will serve as the founding executive director of the Basser Research Center.

Mindy and Jon Gray graduated from Penn in 1992. Jon Gray is the global head of real estate at Blackstone, the investment and advisory firm. Mindy Gray is a member of the executive committee of the Ovarian Cancer Research Fund, Inc.

## A New Tradition in the Making?

At the Commencement ceremonies in May, members of the Class of 1962 stood and put their hands out to the graduating students to symbolize the transition they were making.

## Therapy with Modified T Cells Shown to Be Safe

HIV patients treated with genetically modified T cells remain healthy up to 11 years after initial therapy, researchers from the Perelman School of Medicine reported in *Science Translational Medicine*. The results provide a framework for using this type of gene therapy as a powerful weapon to treat HIV, cancer, and a wide variety of other diseases.

"We have 43 patients and they are all healthy," says senior author Carl June, M.D., a professor of pathology and laboratory medicine. "And out of those, 41 patients show long-term persistence of the modified T cells in their bodies."

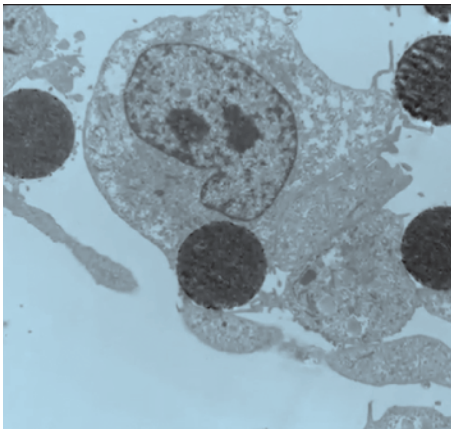
Early gene therapy studies raised concern that gene transfer to cells via retroviruses might lead to leukemia in a substantial proportion of patients, because of mutations that may arise in genes when new DNA is inserted. The new long-term data, however, allay that concern in T cells, further buoying the hope generated by work June's team published in 2011 that showed the eradication of tumors in patients with chronic lymphocytic leukemia using a similar strategy.

"If you have a safe way to modify cells in patients with HIV, you can potentially develop curative approaches," June says. "Patients now have to take medicine for their whole lives to keep their virus under control, but there are a number of gene therapy approaches that might be

curative." A lifetime of anti-HIV drug therapy, by contrast, is expensive and can be accompanied by significant side effects.

The approach the Penn Medicine team studied may allow patients with cancers and other diseases to avoid the complications and mortality risks associated with more conventional treatments. Unlike cancer patients who receive stem cell transplants, patients treated with the modified T cells did not require drugs to weaken their own immune systems in order for the modified cells to proliferate in their bodies after infusion.

To demonstrate the long-term safety of genetically modified T cells, June and colleagues have followed HIV-positive



patients who enrolled in three trials between 1998 and 2002. Each patient received one or more infusions of their own T cells that had been genetically modified in the laboratory using a retroviral vector. The vector encoded a chimeric antigen receptor that recognizes the HIV envelope protein and directs the modified T cell to kill any HIV-infected cells it encounters.

The project was supported by a grant from the National Institutes of Health (1U19AI082628), the University of Pennsylvania Center for AIDS Research, and the Infectious Diseases Clinical Research Program, a Department of Defense program funded in part with federal funds from the National Institute of Allergy and Infectious Diseases under Inter-Agency Agreement Y1-AI-5072.

– Holly Auer

## Honors & Awards

**Jean Bennett, M.D., Ph.D.**, the F. M. Kirby Professor of Ophthalmology, has been awarded the 2012 Alfred W. Bressler Prize in Vision Science by The Jewish Guild for the Blind. A recent recipient of the National Institutes of Health's Pioneer Award for her innovative approaches to major challenges in biomedical research, Bennett studies the molecular genetics of inherited retinal degenerations in order to develop rational approaches for treating retinitis pigmentosa, age-related macular degeneration, and other disorders. She is also a senior investigator in the F. M. Kirby Center for Molecular Ophthalmology and conducts research at the Center for Cellular and Molecular Therapeutics at The Children's Hospital of Philadelphia.

**Steven Brem, M.D.**, professor of neurosurgery and chief of the division of neurosurgical oncology, received the 2012 Joel A. Gingras Jr. award from the American Brain Tumor Association. Brem, who leads the multidisciplinary Penn Brain Tumor Center, has performed more than 3,600 brain tumor surgeries, has participated in more than 100 clinical trials, and has conducted extensive research in discovery and translation of novel inhibitors of angiogenesis and glioma progression.

**Helen C. Davies, Ph.D.**, professor of microbiology, was honored with a Post-50th Lifetime Achievement Award, presented by the Brooklyn College Alumni Association. She was recognized for her distinguished career and outstanding achievements that have contributed to the living history of Brooklyn College. She is academic coordinator for the Department of Microbiology and formerly served as associate dean for students and house staff affairs in the medical school. She is a recipient of many teaching awards, and her research interests have included the biochemistry of prokaryotic organisms.

**Clifford S. Deutschman, M.D.**, professor of anesthesiology and critical care and director of the Sepsis Research Program, has been named president of the Society for Critical Care Medicine. The society is the largest multiprofessional organization dedicated to ensuring excellence in the practice of critical care. Deutschman cares for critically ill patients as a member of HUP's multi-disciplinary Surgical Critical Care Service.

**Garret FitzGerald, M.D.**, chair of the Department of Pharmacology and director of the Institute for Translational Medicine & Therapeutics, was among 44 Fellows and eight Foreign Members elected this year to the Royal Society. Fellows have included Isaac Newton and Charles Darwin.

FitzGerald, also the McNeil Professor in Translational Medicine and Therapeutics, takes an integrative approach to elucidating the mechanisms of drug action. His body of research contributed substantially to the development of low-dose aspirin as a preventive approach to heart

disease. His group was the first to predict and then explain mechanistically the cardiovascular hazard from NSAIDs. His team was also the first to discover a molecular clock in the cardiovascular system, which has contributed substantially to the understanding of the importance of peripheral clocks in the regulation of cardiovascular and metabolic function.

**Carl June, M.D.**, professor of pathology and laboratory medicine and director of translational research for the Abramson Cancer Center, was named among the top three winners of the Top 10 Clinical Research Achievement Awards of 2012, presented by the Clinical Research Forum. He was recognized for his work in treating chronic lymphocytic leukemia by using genetically engineered versions of the patients' own T cells, which multiply in the body as "serial killer" cells aimed at cancerous tumors. His team's findings, which have drawn a new map for the treatment of ovarian and pancreatic cancers and mesothelioma, were published last August in *The New England Journal of Medicine* and *Science Translational Medicine*. According to the Clinical Research Forum, the work "was among the best and most compelling examples of scientific innovation resulting from the nation's investment in research that can benefit human health and welfare."

With David Porter, M.D., professor of medicine, June was also honored by *Discover Magazine* (January-February 2012). Their work using the genetically modified T cells of the leukemia patients was named by the magazine among the top ten stories of 2011. According to *Discover*, "The trial opens the door for new therapies for thousands of people with leukemia and perhaps, down the road, the millions suffering from other cancers."

Other members of the team were Bruce L. Levine, Ph.D., research associate professor of pathology and laboratory medicine and director of the Clinical Cell and Vaccine Production Facility; Michael Kalos, Ph.D., adjunct associate professor of pathology and laboratory medicine; Adam Bagg, M.D., professor of pathology and laboratory medicine; Sharyn Katz, M.D., assistant professor of radiology; and Stephan Grupp, M.D., Ph.D., associate professor of pediatrics.

**Mark A. Lemmon, Ph.D.**, chair of the Department of Biochemistry and Biophysics, is the 2012 recipient of the Dorothy Crowfoot Hodgkin Award. Lemmon is being recognized for major contributions to the field of signal transduction and transmembrane signaling mechanisms of receptor tyrosine kinases. Crystallographic, biochemical, and genetic studies from his laboratory have provided sophisticated understanding of the epidermal growth factor receptor (EGFR) family and offer new ideas for developing therapies that target cancer and other human diseases.

Noting that the EGFR studies involved the work of Penn postdoctoral and medical students, Lemmon named Diego Alvarado, Daryl Klein, Sung Hee Choi, Jeannine Mendrola, and Fumin Shi – "all great examples of the superb scientists that Penn Medicine attracts and reasons why it's so great to be here."

**Arthur H. Rubenstein, M.B.,B.Ch.**, received the George M. Kober Medal, the highest honor of the Association of American Physicians, at its annual meeting. Since 1925, the association has presented the award for research in scientific medicine that rises to the highest level of achievement. Rubenstein and his mentor Donald Steiner developed the first accurate way to measure insulin secretion in diabetic patients being treated with insulin derived from the pancreas of cattle or pigs. This method was crucial to the commercial production of human insulin for diabetics. Rubenstein and Steiner were also part of a team that discovered the first case of diabetes caused by abnormal insulin. Now professor of medicine in the Division of Endocrinology, Diabetes, and Metabolism, Rubenstein stepped down last summer as dean of the Perelman School of Medicine and executive vice president of the University of Pennsylvania for the Health System.

## Transitions

**Benjamin Garcia, Ph.D.**, has joined the University of Pennsylvania as the first Presidential Term Professor. He is Presidential Associate Professor of Biochemistry and Biophysics in the Perelman School of Medicine and also joins the Penn Epigenetics Program.

"He is a brilliant young scholar and researcher whose pioneering work in cell biology and proteomics has placed him at the forefront of his field, earning him numerous awards, including a Presidential Early Career Award," said Amy Gutmann, Ph.D., Penn's president.

Garcia, who earned his Ph.D. degree in chemistry from the University of Virginia, was assistant professor of molecular biology at Princeton University. His pioneering research involves developing new mass spectrometry methods and bioinformatic computational tools to examine critical

## The Academies Make Their Picks

**Gideon Dreyfuss, Ph.D.**, and **Beatrice H. Hahn, M.D.**, of the Perelman School of Medicine, and **Nancy Bonini, Ph.D.**, of the School of Arts and Sciences, have been elected members of the National Academy of Sciences. Election to the academy is considered one of the highest honors for a U.S. scientist or engineer. Cited for "their distinguished and continuing achievements in original research," the three scientists are part of the 2012 Academy class of 84 members and 21 foreign associates.

Gideon Dreyfuss is the Isaac Norris Professor in the Department of Biochemistry and Biophysics and is also an investigator for the Howard Hughes Medical Institute. His work examines how RNA and associated proteins function in degenerative diseases.

Beatrice H. Hahn is a professor in the departments of Medicine and Microbiology. She studies the origins, evolution, and disease mechanisms of human and simian immunodeficiency viruses.

Nancy Bonini is the Lucille B. Williams Professor of Biology and an investigator for the Howard Hughes Medical Institute. Her research makes use of the fruit fly *Drosophila melanogaster* to identify genes that play crucial roles in human brain disease.

The American Academy of Arts and Sciences elected two faculty members of the Perelman School: **Thomas Curran, Ph.D.**, and **Gary A. Koretzky, M.D. '84, Ph.D.** Curran is a professor of Pathology and Laboratory Medicine. His studies of the molecular basis of brain cell growth have informed new strategies to treat pediatric brain tumors. He also serves as deputy scientific director of the Research Institute at the Children's Hospital of Philadelphia.

Koretzky is the Francis C. Wood Professor of Medicine and vice chair for research and chief scientific officer of the Department of Medicine. Through investigations of the regulation of blood cell formation and movement, Koretzky has made inroads into understanding the complexities of immune system function.

modifications in cellular proteins that alter and control their functions.

According to Shelley Berger, Ph.D., director of the Penn Epigenetics Program, "Garcia is particularly interested in protein changes at the 'epigenetic' level – that is, control beyond the DNA sequence, as influenced by the environment and diet. Thus, the advances he is making have crucial implications for medicine and bioengineering and will nucleate a great deal of interdisciplinary work involving investigators across the University of Pennsylvania"

**Frances E. Jensen, M.D.**, has been named chair of the Department of Neurology, effective August 13, 2012. A professor of neurology at Harvard Medical School, Jensen is director of epilepsy research at Boston Children's Hospital. She is also director of translational neuroscience at Children's Hospital and a senior neurologist at both Brigham and Women's Hospital and Children's Hospital.

The primary focus of Jensen's research has been to investigate pathophysiological mechanisms of epilepsy as well as secondary effects on synaptic plasticity. She has also been exploring age-dependent differences in such mechanisms, with special attention to the interactions among brain development, excitotoxic brain injury, epilepsy, and cognition. Most recently, supported by a five-year Director's Pioneer Award from the National Institutes of Health, Jensen has been investigating connections between epilepsy and autism, examining how seizures in early life alter neuronal networks in the developing brain to cause cognitive disorders such as learning deficits, neuropsychiatric symptoms, and autism. As she told *Nature Medicine* last year, "We are finding connections between previously assumed unrelated disorders that we could never have imagined."

Jensen is also the sponsor of an FDA-approved "investigational new drug" for a continuing multi-center clinical trial of a novel therapy for neonatal seizures, based on basic research in her laboratory.

Currently president of the American Epilepsy Society, Jensen has served in several review and council positions for private foundations and the National Institutes of Health. She is also known as a dedicated and inspiring teacher and mentor, with a strong record of placing postdoctoral trainees in faculty positions at competitive academic medical institutions and universities.

Jensen received her medical degree from Cornell University Medical College. She was chief resident in neurology at The Harvard Longwood Neurology Training Program.

# Investigating the Mysteries

By Marshall A. Ledger

**Daniel Rader** is changing the paradigm, redefining the problem, and seeking new ways to regulate cholesterol mechanism.

There's "good" cholesterol and there's "bad" cholesterol. Raise the good and lower the bad. What could be plainer, more direct? The words even carry moral authority. In a world where medical science is rarely definitive, here is an easy-to-follow health directive to reduce the risk of atherosclerosis and other heart diseases.

Then comes Penn Medicine's Daniel J. Rader, M.D., prominent among his peers for his work on cholesterol metabolism and familiar to the media as one of their go-to experts for commentary when the topic makes news. He has helped muddy at least part of that tidy formula.

The bad stuff is still bad – the lower our LDL, the better – but its full story is still unfolding. "Honestly," Rader says, "a decade ago we thought we pretty much understood most of what existed about the regulation of LDL levels," but that complacency is gone.

His chief concern is with HDL, which is still good, but not as absolute as the term sounds. "It's nuanced," he says. "As we learn more and more, it's not completely clear that all HDLs of any type are good. There may be more to it than that."

Readers of the front page of *The New York Times* on May 17 saw the report of a new study that builds on the work Rader has been doing on HDL – and for which Rader was a co-author. According to the lead author of the study, Benjamin F. Voight, Ph.D., assistant professor of pharmacology at Penn, "Through our research, we have found that all roads that raise HDL do not always lead to the promised land of reduced risk of heart attack."

In addition to a new hypothesis about HDL, Rader's work has helped lead to the discovery of a new gene, the creation of an assay that is now widely used, and the application of a discarded drug to help a certain group of under-served patients.

He has been recognized for his achievements. He holds an endowed chair as the Edward S. Cooper, M.D./Norman Roosevelt and Elizabeth Meriwether McLure Professor of Medicine.

As a researcher, he has received coveted, long-term funding in grants that come with such labels as "Freedom to Discover," "Distinguished Clinical Investigator Award," "Networks of Excellence," and "M.E.R.I.T," i.e., "Method to Extend Research in Time."

As a clinician, he has been recognized as a "top doc" in national listings as well as in *Philadelphia* Magazine, where he has appeared every year for more than a decade, and he has won teaching awards in the School of Medicine and his department.

He regularly delivers invited lectures at other universities, serves on committees of national organizations in his field, and

engages in editorial and peer-review activities for general and specialized journals in medicine. He also co-founded and serves on the board of Vascular Strategies LLC, a company focused on treatments for cardiovascular disease.

Last year, he was one of 70 in the country elected to the Institute of Medicine "for excellence and professional achievement."

"He certainly is a world leader in lipoprotein metabolism," says one of his first mentors, Julian B. Marsh, M.D. '47, "but he is still not at the apex of his career."

# of Cholesterol

## Before cholesterol gained cachet

Rader was unwittingly introduced to his field as a student at the Medical College of Pennsylvania in the early 1980s, when he worked in Marsh's laboratory there.

At that time, Marsh was professor and chair of physiology and biochemistry at M.C.P. (he had held a comparable position at Penn, in both the School of Medicine and the School of Dental Medicine). He is one of the deans of lipoprotein metabolism, and Rader was interested in gaining experience from a proven scientist, more so than in entering that specific field.

He stood out: "He was very enthusiastic, learned quickly, and had a very good mind. You could tell at that time he was going to do well," says George H. Rothblat, Ph.D., then an M.C.P. biochemist who would later collaborate with Rader on some major projects.

Although Rader showed potential, the field promised less. "Cholesterol was still a backwater," Rader recalls. There were no statins to lower cholesterol (the first would appear in 1987), and the best drugs available – niacin and bile acid sequestrants – had many side effects.

Even more, "we didn't have any evidence that treating cholesterol actually lowered cardiovascular risk," he says, "so the times were very different."

Rader had just started his residency at Yale-New Haven Hospital in 1985 when Michael S. Brown, M.D. '66 and Joseph L. Goldstein, M.D., won the Nobel Prize for their discoveries on how LDL works. Their work, says Rader, was "certainly inspiring to the field. It started to give some real molecular underpinnings to our understanding of why certain people have high cholesterol. But it was still a long way off from a vision of treatment of cholesterol as a way of reducing cardiovascular risk."

## "I wonder if . . ."

After his residency, Rader went directly to work in the laboratory of H. Bryan Brewer Jr., M.D., at the National Institutes of Health. The move was a bit atypical, because Rader had no subspecialty training in cardiology or endocrinology. But he learned a lot of basic science and treated patients – "what we now call translational research," he says – and he knew he wanted to pursue a career that included both bench investigations and patients.

In Brewer's lab, Rader began strands of research that he would continue at Penn. He studied the metabolism of HDL in humans – why some people have especially high or low levels of HDL – and helped define some genetic mutations that affected the metabolism and thus HDL levels.

He also worked on a subclass of lipoprotein abbreviated as LP(a). Although discovered in 1963, it did not interest scientists for decades, so little was known about it. Rader was part of the Brewer team that published studies on the metabolism and regulation of LP(a) levels, contributions to the field that are still cited.

Now, he says, interest in LP(a) is "through the roof." LP(a) turns out to be an unusual lipoprotein because it ranges from almost undetectable levels to nearly 1,000 mg/dL (milligrams of glucose per deciliter of blood, but the unit tags for cholesterol levels are rarely used in ordinary conversation). As Rader puts it, that is "a huge range, almost all genetic, and it's an independent risk factor for heart disease."

The Brewer group was also looking for the gene that underlies a rare disease of essentially zero LDL, abetalipoproteinemia. Rader followed many of the N.I.H.'s patients with this disorder, and one day he attended a talk by a colleague describing his new discovery, a protein in the liver of cows.

Afterward, Rader chatted with the speaker and wondered aloud if the protein could be the defect compound in abetalipoproteinemia. The two scientists and others joined in a collaboration that ultimately showed that the gene *MTP* was mutated in patients with this disease.

## Building a lab

After nearly six years at the N.I.H., Rader decided to move to a more traditional academic environment with medical students and patients in a regular hospital setting. He knew that Philadelphia ("surprisingly") did not have a major presence in the cholesterol field, so he inquired at Penn. ("A lot of recruitment is very serendipitous," he observes.)

At Penn, Rader would be close to Lancaster, Pa., where he grew up, and he'd be able to start a lipid clinic and an HDL research program. In addition, Penn was getting into gene therapy, which he thought might prove beneficial for the LDL-receptor deficiency that Brown and Goldstein had identified and that causes the disease of excessively high LDL, known as familial hypercholesterolemia.

In 1994, when Rader arrived at Penn, the foremost HDL hypothesis was that raising HDL levels would reduce cardiovascular risk. "That's what the epidemiology taught us, and that's what the animal models taught us," he says. Others – individuals and companies – were interested in developing drugs, but gene therapy seemed promising. "Frankly," he says, "there was a lot we didn't understand about what fundamentally regulated HDL levels and why some were high and some were low."

Rader thought he and his team could learn from patients with unusually high numbers (80 for a man and 90 for a woman would put the individual in the top 5th percentile). Today Penn has the largest population of these patients in the world, which helps Rader's lab sort out both the genes that cause high HDL and its effect on cardiovascular risk.

Rader's team includes three former colleagues from the Medical College of Pennsylvania who now are Penn research professors of pediatrics based at The Children's Hospital of Philadelphia: Sissel Lund-Katz, Ph.D.; Michael C. Phillips, Ph.D., D.Sc.; and Rothblat. (A fourth, the late Jane M. Glick, Ph.D., had taught Rader in medical school and come to Penn about when he did; she helped him set up the lab.)

Asked what Rader adds to a research project, Rothblat says: "He's extremely bright, he has a fantastic memory and

## Dan Rader as Translational Strategist

Photograph by Daniel Burke

If you look up Daniel J. Rader on Penn's Web site, you find, among summaries of his research initiatives, a daunting list of administrative appointments. I hand him a copy of the list as a way of asking how he fits these into his life. He immediately notices a few omissions – the list is outdated, it should name even *more*. But it has a general thrust fully harmonized with his work in his lab and clinics: translational medicine.

Translational medicine is a bridge between lab discoveries in biomedical science and the development of new therapies for patients. Its hub at Penn Medicine is the Institute for Translational Medicine and Therapeutics, an intellectual home to more than 800 investigators from Penn and surrounding institutions.

ITMAT is also the "world's first such institute, in the sense that we gave form to a disciple that was in evolution and has now proliferated to every academic medical institution in the country and many in the world," says its director, Garret A. FitzGerald, M.D., professor of medicine and pharmacology, chair of pharmacology, and the McNeil Professor in Translational Medicine and Therapeutics.

To illustrate how a translational researcher works, Fitzgerald notes how Rader has elucidated the functional significance of genes associated with cholesterol. "That's a model," he explains, "because, up to now, the people involved in gene discovery have been a different tribe of people from the people interested in gene function. What Dan has done provides the translational glue between those two tribes."

In his administrative roles, Rader often serves as a strategist. His key appointment is associate director of Penn's Institute for Translational Medicine and Therapeutics; he is chief of a comparable division in the Department of Medicine. And he is leading the development of a comprehensive biobank at Penn Medicine.

He is also the liaison between his cardiovascular labs, on the 11th floor of the Translational Research Center, and a diabetes research unit on the floor above. He reaches for my sheet of interview questions. Turning it over for blank space, he draws two overlapping circles, one for cardiovascular research, the other for diabetes research. The overlap represents vascular disease, which, he notes, is a major problem for patients with diabetes. He heads the effort that seeks opportunities for the areas to interact.

### A useful concept

Has the emergence of the term *translational medicine*, first used in 1993, furthered the goal?

knowledge of the field, he can synthesize hypotheses and design appropriate experiments to test the hypotheses. He's a really fine investigator."

His mentor Julian Marsh puts it this way: "If you had to use one word to describe Dan, it would have to be *brilliant*." He adds: "No matter how bright and how much the top scientists achieve, it's very, very difficult for them to succeed at very high levels unless they are very good at interpersonal relationships – and that's another area where Dan is a standout."

All of those qualities, and his achievements, have brought Rader impressive funding: for instance, a National Institutes of Health M.E.R.I.T. Award; an award of nearly $15 million under the American Recovery and Reinvestment Act of 2009 for the Complex Genetics Initiative (Rader is the principal investigator); a $9-million N.I.H. grant for stem cell research with Penn's Edward Morrisey, Ph.D., professor of medicine and of cell and developmental biology, and Stephen A. Duncan, Ph.D., at the Medical College of Wisconsin; and a 5-year, $6-million grant from the Paris-based Fondation Leducq.

These awards have helped drive his laboratory, which takes up the 11th floor of the Translational Research Center, some 45,000 square feet of offices and lab space with some 25 investigators and others. As we walk through, he calls out "So, did it work?" to a pair of researchers hunched over some equipment at a workstation.

They look up in surprise and laugh. "We're about to find out," one of them says. "Just took a protein reading."

Rader extends a thumbs-up sign, says, "All right, all right!" and we move on.

The Translational Research Center, with seven floors of labs in all, is adjacent to the Perelman Center for Advanced Medicine, a clinical building. (For more on "translational," see the box on page 8.) "Part of the idea," says Rader, "is to encourage interactions between clinicians and scientists and among scientists of different disciplines, so that we can have these serendipitous kinds of conversations that lead to new discoveries."

## Function rather than level

One of the Rader team's major pursuits is what he calls the "nuanced" sense of HDL. As he explains the metabolic process, the liver makes cholesterol, and LDL transports it to blood vessels, which take it up. One of HDL's main functions, goes the hypothesis, is to interact with the plaque in the blood vessels, extracting the cholesterol and returning it to the liver, where the body excretes it.

The process is formally known as "reverse cholesterol transport," but Rader calls it "efflux." "It's an elegant, overly simplistic concept," he says, "but it's part of what we think HDL does to make HDL protective."

**Efflux is "part of what we think HDL does to make HDL protective." Rader's team is now developing therapeutic approaches to promote HDL efflux.**

As the basic scientists extracted cholesterol from cells and Rader contributed the animal models and patients, the team developed a novel method to measure efflux. They took cells from mice and inserted a cholesterol "tracer" that can be followed as it moves in the body. Then they injected the cells back into the mice in order to trace the movement of the cholesterol from the cells' macrophage to the liver and out into the feces. The procedure, in use for some six years now in more than two dozen labs around the world, is often referred to as the Rader Assay.

It has also helped confirm the efflux hypothesis – just when some new drugs that raised HDL proved to be failures in reducing the risk of heart disease. *The New England Journal of Medicine* published the Rader group's results in 2011. They are now developing and evaluating the effect of new therapeutic approaches that will promote HDL efflux.

"New therapies to bolster the good cholesterol and allow the body to naturally cleanse itself of the bad cholesterol are the new frontier," observes Richard P. Shannon, M.D., the Frank Wister Thomas

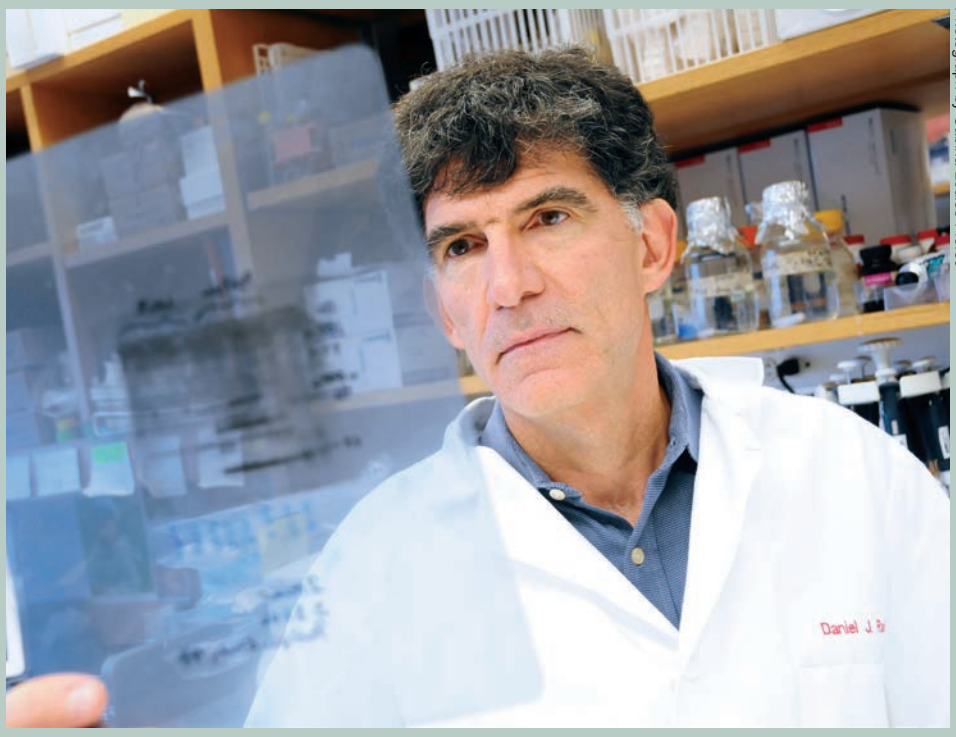
"It's become a bit of a buzz word," Rader acknowledges, "but I think it's helpful, especially for junior people. They need to have a sense of a viable career path."

For instance, they know they can have careers as bench scientists, or do clinical trials as part of a clinical career in academe, or enter epidemiology, engaging in longitudinal projects such as the Framingham Heart Study.

"But translational medicine – where you do detailed, mechanistic studies in humans, often linked to laboratory-related research in service to that – had never been a defined career path before, so there's an advantage in defining it.

"First, if you've defined it, people know what you're talking about – it's a useful term. Second, it defines a career path for younger people. They can point to it and see steps they can follow to get into it and the training they'll need, and realize they could be an investigator who sits on this cusp between the bench and patient care, doing studies on humans to try to advance our understanding of disease. That's really the major utility of it."

– Marshall A. Ledger



Photograph by Sabina Louise Pierce

Professor of Medicine and chair of the Department of Medicine, where Rader is based. "Dan is the foremost figure in the translational approach to HDL as a therapeutic target."

One route could be gene therapy, for which Rader and his team, along with the late Michael Jaye, Ph.D., then at the pharmaceutical firm Rhone-Poulenc Rorer, took the crucial first step. They found a gene – an enzyme called endothelial lipase – that is important in regulating HDL metabolism and HDL levels; they confirmed the gene's functions in mice and subsequently in patients with high HDL.

They went on to find a variant that occurs in about one percent of the population; the mutation inactivates the gene and raises HDL. Next, they joined in a collaborative study of more than 100,000 people and verified the finding.

Because these people had high HDL, Rader reasoned, they should have had a lower risk of heart disease – but that's not what the investigators found. "It was somewhat disappointing," he says, "but it circles back a bit to what I said: Maybe it's not just the HDL level, we also need efflux.

"So in that vein, we continue to use human genetics – that is, sequencing other genes and even whole-genome approaches – to look for genes that impact on HDL levels. Our goal is to find some genes that actually raise HDL levels *and* seem to protect against heart disease, and our hypothesis is that they'll also promote the efflux. This is work in progress."

## A new role for academe in drug development

Meanwhile, Rader has resumed another strand of work that dated from his arrival at Penn. In the mid-'90s, he started to explore gene therapy to treat patients with familial hypercholesterolemia, or FH, which causes excessively high LDL – over 500. Two of his five patients had modest LDL reductions, but he stopped the work because the results were inconsistent.

A few years later, he resumed it. Several of his former colleagues, who had moved from government and academe to Bristol-Myers Squibb, were trying to develop a drug that targeted the protein whose mutations made LDL abnormally low; such a drug, they surmised, would help people with high LDL.

Rader led a proof-of-concept study and showed that the drug lowered LDL from 190 to about 70. But the drug gave some patients gastrointestinal side effects such as diarrhea, and it raised the fat in the liver, so the pharmaceutical firm stopped the program.

But Rader considered the situation of his patients with FH: They get heart disease as children and generally die of cardiovascular problems before the age of 30. With those dire prospects, he figured the side effects could be managed, so he applied for the rights to the drug.

"There was a fair amount of discussion," he says, "but at the end, to their credit, Bristol-Myers Squibb transferred the intellectual property of the drug to Penn to further develop."

With a Doris Duke Charitable Foundation grant to pursue his idea, and with six patients, Rader showed that the drug reduced LDL by fifty percent – "which in this disease is pretty much unheard of."

FH qualifies as an "orphan disease," meaning that there are fewer than 200,000 patients with the condition in the United States. Drug companies generally aren't interested in disorders with small markets, so the Food and Drug Administration sometimes steps in with funding, which Rader received. Such diseases follow a different path to approval than that used for mass-market medicines. He and his team filed a new drug application in February and hope to hear of approval by the end of the year.

Rader has mitigated the drug's GI side effects by starting the dose low and titrating it over time, and by counseling on diet. Experiments suggest that higher liver fat might not be problematic. After rising, it plateaus, and "might even start to come down a bit," he says, "so it won't be a problem for these patients at least."

Then he muses: "It's an interesting rescue of an abandoned drug." He explains that there is growing interest in drugs that fail because of safety, tolerability, or efficacy but that may be repurposed for specific groups of patients who would otherwise get no treatment at all. Rader notes that Francis S. Collins, M.D., the head of the National Institutes of Health, has declared an interest in this area.

Indeed, since Rader and his group completed their work, the Perelman School of Medicine has established the Penn Center for Orphan Disease Research and Therapy (see *Penn Medicine*, Fall 2011). It offers the prospect of finding therapies for orphan diseases on a large scale, and Rader is optimistic.

"It's a fantastic role for academe in drug development," he says. "We don't do certain things that the drug industry does very well – make the molecules, for instance. But we have the patients, we understand these rare diseases very well, we understand what is needed to approach them, and we have the motivation to look for drugs that might be useful for particular rare-disease application and get them to these patients."

## Optimism about gene therapy

Meanwhile, Rader continues to seek new and better ways to target the liver for gene therapy, collaborating with James M. Wilson, M.D., Ph.D., professor of pathology and laboratory medicine, and using techniques Wilson has pioneered. As part of an N.I.H.-funded initiative, Rader and others have shown that vectors, or delivery systems, using the adeno-associated virus can be used against FH.

In March, Rader was the "sponsor" of a group that presented a protocol to the Recombinant DNA Advisory Committee at the N.I.H. (The "sponsor" has the regulatory role of overseeing the principal investigator and making sure the research is carried out properly.)

Eventually, Rader feels, FH patients will receive the gene therapy, which will lower their cholesterol but not normalize it, and receive the drug that targets *MTP*, the gene Rader had studied earlier, which will reduce cholesterol further. "The combination of those two, I think, will convert this disease that is almost invariably fatal by the age of 30 to a chronic manageable disease."

Genetics is likely to play an even greater role in finding new pathways that regulate cholesterol metabolism. Rader and his group are involved in the global effort to use "genome-wide association studies," which scan the entire human genome for common variants that might be related to a particular disease. As he says, "It's an open-ended, unbiased way of asking, 'What other genes are out there that we don't know about yet that impact on my disease of interest?'"

**In academic medicine, "we understand these rare diseases very well, and we have the motivation to look for drugs that might be useful for particular rare-disease application."**

Two years ago, he was part of a team that published a piece in *Nature* identifying 95 different areas of the genome associated with LDL and HDL, most previously not known. To Rader, that's a start toward understanding the biology of how the genes work on cholesterol.

One new finding was the gene *Sort1*, which encodes the protein sortilin. Investigators at Penn (including Rader) and elsewhere figured out how it regulates LDL. It is, he says, "a whole new pathway. That might be a target for new drug development, we don't know – but it's certainly new biology."

## So much discovered, so much to discover

What does Rader see when he places his HDL research into the field's historical picture? "We are with HDL where we were with LDL a few decades back: a lot of interesting information, epidemiology, basic science, but complete uncertainty about whether targeting HDL from a therapeutic standpoint is actually going to reduce cardiovascular risk."

So, yes, he's amazed at the amassed knowledge, "but it's a different kind of amazement, that we haven't made more progress. We've learned a lot, but we have a long way to go."

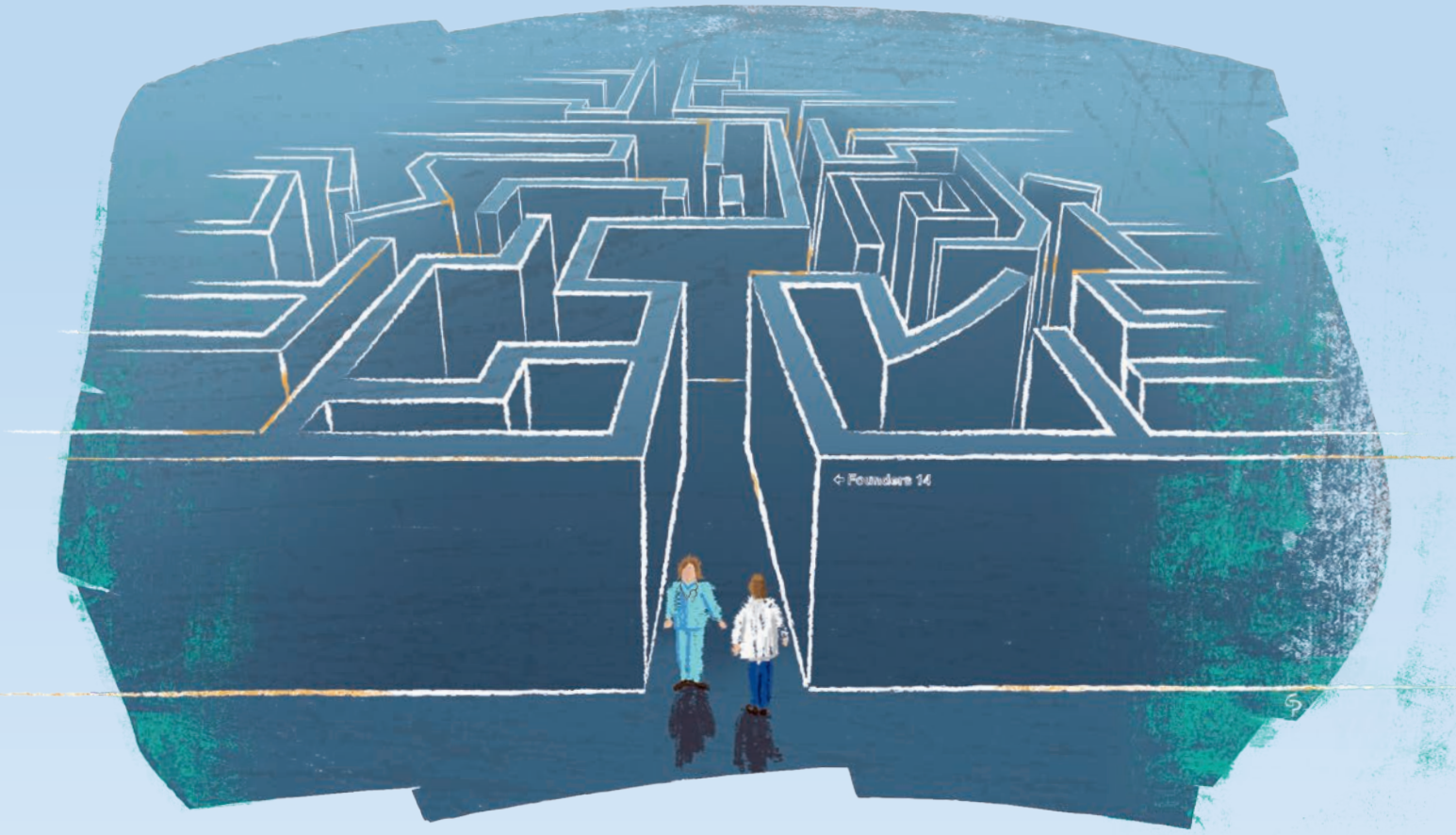
He mentions the hard-won certainty that lowering LDL reduces cardiovascular risk. "Believe me, in the mid-'80s, that was nowhere near a tenet of faith" despite the 1985 Nobel Prize in the field, he says. "Even in areas of science that we think we understand, there are new things to be discovered."

Richard Shannon, the chair of medicine, agrees: "The discoveries that have been made in this era of genetics and genomics and molecular biology have opened entirely new opportunities to target new molecules in cells that contribute to disease – and there are thousands of these targets. Investigators working in teams to target these abnormalities through new kinds of therapeutics – that's the real opportunity."

And that's an important concept for medicine at large, Rader adds. "It's common, particularly among young trainees, to feel that most of the important things have already been discovered. Nothing could be further from the truth. There's so much we have yet to learn. The cholesterol field is a microcosm for that." ●

# Those First Days in Clinical

*By Sally Sapega*




## A new nurse mentor program helps medical students learn the ropes.

Like a deer in the headlights.

That's how Stuart Carter, a student at the Perelman School of Medicine, described how he felt when he began his first clinical rotation at the Hospital of the University of Pennsylvania in early 2011. "It was scary, trying to navigate the system," he said. "Especially Founders 14, which is a fast-moving, well-oiled machine."

Enter Diana Santangelo, B.S.N., R.N., a clinical nurse who participates in a new program that focuses on interdisciplinary education and pairs nurses with medical students coming to clinical rotations. Remembering the fear that she felt on her first clinical rotation as a student nurse, Santangelo took the time to show Carter not only the ins and outs of the unit but also the important roles nurses play in patient care. Looking back, said Carter, "It was nice to have someone help ease my burden. Now I feel much more comfortable interacting with the nursing staff."

To a great extent, the new program is an extension of Penn Medicine's Unit-Based Clinical Leadership initiative, which began in 2007. The UBCLs are three-way partnerships that manage quality in the Health System's hospital units, led by a physician leader, a nurse leader, and a project manager for quality. These interdisciplinary groups have demonstrated the immense benefits when health-care professionals work as a team instead of in side-by-side silos. The mentoring program brings them together as

# Frightening Rotation

well, but at an earlier stage – and the results show great promise for the patients and for the professionals themselves.

## Structuring the Program

Betty Ann Boczar, B.S.N., nurse manager of Founders 12 and 14 and one of the first nurse managers to implement the UBCL model, and Kate FitzPatrick, M.S.N., R.N., clinical director of Nursing Operations and Women's Health at HUP, were brought into the mentoring program early in the planning process. Both credit Victoria Rich, Ph.D., chief nurse executive of UPMC, as "the visionary" who initiated the program with Stanley Goldfarb, M.D., associate dean for curriculum in the School of Medicine, as well as other medical school faculty members and administrators.

As Rich put it at a recent campus symposium on interprofessionalism, in programs like UBCL, "we role-model what we believe in." In the past, she noted, there was sometimes insufficient trust among the hospital practitioners, and some professionals who worked side by side did not know each other's expertise.

According to Goldfarb, "Medical students had no idea of the various roles of nurses, and nurses didn't know how much the students knew – what their background would allow them to do. It's two different worlds coming together."

Input from groups of nurses and medical students helped shape the structure of the mentoring program, said Anna Delaney, chief administrative officer of academic programs at the School of Medicine. "We asked them, 'What is it you don't understand about each other? What has worked well and what hasn't?'"

Based on the responses, "we developed a checklist of nursing actions that we felt were important for a medical student to see," said Jennifer Kogan, M.D. '95, associate professor of medicine. The actions included admitting and discharging patients, caring for wounds, and administering medications.

## What Does a Nurse Do?

Although medical students receive classroom training in clinical areas, their knowledge about the flow of the hospital and how a patient unit works is often minimal. "Diana was the point person I could direct questions to," said Stuart Carter. "She showed me the structure of the floor, the different roles of nurses, support staff. . . . I had a much better perception of who to go to for answers and as a result I was a more helpful med student."

In Santangelo's view, the biggest surprise was how little medical students seem to know about the role of the nurse in patient care. "Sometimes I feel like they think things magically happen!" she said, laughing. "I tell them, 'These are the steps we have to do to prepare for a discharge . . . so be nice to me when you're an intern and I call you 15 times!'"

"The process from the doctor typing an order into the computer to its execution is like an algebra equation – many factors play into it," explained Ian Villarreal, B.S.N., nurse mentor on Founders 14. For example, when administering medication, "we have to know 'Can the patient swallow? If there are two meds, are they compatible?' . . . There are a lot of subtleties to be learned."

## A Treasure Trove of Information

Wound care on a patient with diabetic foot ulcers. Pulling together information for a patient discharge. "These are things you never see when you're with a resident or attending," said Ivor Asztalos, a Penn medical student who was in the mentor program. But, what's even better, he said, is knowing where all that information is charted online. "It's a treasure trove of information. And it's not only great information but there's also electronic charting for information that's frequently difficult to acquire, like a patient's daily intakes and outtakes or weights."

> "She showed me the structure of the floor, the different roles of nurses, support staff. . . . I had a much better perception of who to go to for answers."

As Asztalos learned, the nurse's information can also help confirm findings. "Pre-rounds with residents are directed at information pertinent to the organ systems involved. For example, if it's a heart patient, we look for edema, check the heart and lungs. But nurses do a head-to-

Photo by Sally Sapega

As a nurse mentor, Diana Santagelo shows Stuart Carter the ins and outs of her unit.

toe assessment every day," he said. "This information can help confirm a finding, but the average med student may not know this information even exists . . . or how to find it."

Asztalos also learned about the Navicare tracking system. "If patients aren't in the room, where are they? With Navicare, I know if a patient is in transit, on the way back. I don't have to waste time trying to find out."

Villarreal serves as a mentor for his assigned medical student but will take others under his wing when he's tackling one of the checklist items. "I just call out, 'Hey, want to watch an interesting wound change?' and two or three eager students will follow me."

The biggest challenge, said Villarreal, is finding a time when nurses are performing their patient-care activities and medical students are able to watch. "We're hoping to get a day where a med student will only shadow you – no other responsibilities. Right now we try to grab them when we're doing something on the checklist, but they're not always available."

Others in the program have also found the timing to be a challenge. "We're going to recommend that time be set aside on all mentoring units so students can spend several hours with their mentor," said Keith Hamilton, M.D., associate director of the internal medicine clerkship.

## Success Leads to Expansion

The mentor program recently won the Dean's Award for Excellence in Medical Student Teaching by an Allied Health Professional, one of the School of Medicine's annual teaching awards. According to the school, the program is "perhaps the only in the country" of its kind. Boczar and FitzPatrick received the award at the graduation ceremonies of the Perelman School of Medicine in May. Receiving the honor certainly has not stopped its leaders from trying to make the program even better. "It's an ongoing process," said Kogan. "We have to remain flexible and willing to make changes."

Based on the positive response, Hamilton said that every student who does a rotation in internal medicine will now take part in this interdisciplinary process. Since the program was piloted last year on Founders 12 and 14, it has expanded to include Founders 8 (the CCU) and Labor & Delivery, as well as the Acute Care for Elders unit at Penn Presbyterian and one of its floors devoted to general internal medicine. "Each unit we choose brings something unique to the table," Hamilton said. "For example, CCU nurses have expertise in reading telemetry, and the ACE unit demonstrates the nuances in caring for the elderly."

J. Larry Jameson, M.D., Ph.D., dean of the Perelman School and executive vice president of the University of Pennsylvania for the Health System, lent support for initiatives like the mentoring program at the recent symposium on interprofessionalism. He began his welcoming remarks with what he thought would be a familiar story to some of members of the audience. He recounted his first night on call as a resident, acutely aware of what he didn't know. When the nurse came to him and informed him that Mrs. Smith was having chest pains, he said, "I've *read* about this!" And when the nurse made a suggestion for the patient's treatment, he said, "Great idea!" His own experience, he implied, supported a mentoring program that would better equip medical students and new residents, and he acknowledged the promising efforts of Boczar and FitzPatrick.

From Boczar's perspective, there is certainly room for expansion. "Eventually we want to roll this program out throughout the Health System," she said. "We're already getting requests from the surgical units."

As successful health care becomes increasingly dependent on teamwork, said Hamilton, "it's crucial for medical students to understand the roles of other members of the team. When they graduate, they will be helping to lead these teams. It's important to 'grow up' in this environment." ●

# A Matter of Heart

After being stricken at home and flown by helicopter to HUP, a nine-months-pregnant woman had to face other daunting medical challenges.

*By Nefertari Nelson-Williams*

*Photographs by Jon Perlmutter*

**It was June 8th, 2008. I was pregnant, relaxing in my New Jersey home while watching some television, when it happened.**

As I was resting on my deep couch, I felt a pain stronger than I had ever felt before. Since this was my fifth pregnancy, I knew it wasn't labor. I rolled onto the floor but the pain disappeared, leading me to believe it was gone for good. Although I had called the doctor, I quickly called back and said I was fine and started back to my couch.

Suddenly it hit. It was just like they had explained. It felt like a piano or an elephant was sitting on my chest and I wanted nothing more than to remove it so I could get just one breath of air. I sensed movement around me, but the next thing I remember was my husband getting me to the car and rushing me to the hospital. When I arrived, the nurses quickly got me back to labor and delivery. The doctors were puzzled. They were unable to diagnose my problem, which meant I sat in a hospital room for hours without care. I felt every pain and even though

Nefertari Nelson-Williams with her youngest child, Shayna.

they gave me strong pain medication, it didn't help with my inability to breathe.

The next morning finally came. The man who walked in and introduced himself as a cardiologist is still, today, one of my heroes. He said he thought he knew what was going on and that he had ordered a helicopter to take me to the Hospital of the University of Pennsylvania. I was pretty drugged but I do remember hearing voices. The next thing I knew, I was in HUP's Critical Care Unit with hundreds of tubes and doctors surrounding me. I looked up and one of the doctors said in a warm and caring voice, "You are a very sick lady. You are alive, but we need to decide if we are going to spare you or your baby. You and your husband have to make a decision."

I refused to decide. I could feel my baby moving and thumping around just as her four siblings before her had done. Although I knew I had four children at home that needed me, how could I just spare my own life and not give this new beautiful life a chance?

This was a Monday. Every day following, I had dozens of doctors and nurses coming in to visit the woman who had actually survived a coronary artery dissection. Yes, my coronary artery had broken completely in half, and the time that I was left untreated caused the bottom front of my heart to die. It was an actual heart attack. I was experiencing cardiomyopathy (an enlarged heart), and the dead heart muscle was forming an aneurysm that could rupture at any moment. I was a walking time bomb. All of this – and still nine months pregnant.

During one of the daily visits from the crews of doctors that wanted to examine "the sickest woman in the hospital," I looked to my right to see a petite, beautiful blonde storm in as if she had been attempting to reach my room for days. She immediately announced that she was not going to lose me or my baby . . . not on *her* watch. She introduced herself as Dr. Michal Elovitz, doctor of maternal fetal medicine (I believe), and she came close to my face. I looked up into her blue eyes with tears in my eyes and said, "I don't know where you came from or who you are . . . but I know because you are here, everything is going to be all right." She caressed my face and ordered everyone out of my room, making demands for accommodations for her to be at the hospital until the baby was delivered.

> "I had dozens of doctors and nurses coming in to visit the woman who had actually survived a coronary artery dissection. Yes, my coronary artery had broken completely in half, and the time that I was left untreated caused the bottom front of my heart to die. The dead heart muscle was forming an aneurysm that could rupture at any moment. I was a walking time bomb."

The week went on. I received several visitors and my husband sat by my side. I had the world's *best* nurses. I received hugs, kisses, and encouragement daily. It was Saturday, June 14, which just so happened to be my mother's birthday. She had suffered a massive stroke four years earlier and was unable to be there with me because of her own disability. My coworkers were visiting when I felt a cramping at the bottom of my belly. Although my co-workers were working overtime to bring a smile to my face by telling inappropriate jokes, they could see that I was in pain and informed my nurse.

The next thing I knew, I was surrounded by at least 15 doctors and nurses. I had been placed in a glass room with collapsible walls for just this reason – a quick and easy trip to the operating room. When I opened my eyes, I saw those same blue eyes staring at me. Her hair was in a pony tail and she had on a sweat shirt and jeans, and I was able to smile as I touched her sloppy ponytail. She said, "Yes, I've been sleeping here waiting for this moment, and I knew it was going to be today." (I had told her it was my mother's birthday.) We arrived in the operating room and they set me up. She had never delivered a baby vaginally in that operating room. We were praying that today would be the first.

As I lay there, I was being pumped with blood and IV in almost every part of my arm. I was instructed not to push. At that point I was 10 centimeters dilated (the point when the baby should descend) and nothing was happening. Because I had been given so much blood, my heart began to shut down and my lungs filled with fluid. It felt like when you are swimming and you accidentally get water in your nose. I was drowning in my own fluids.

Not on Dr. Elovitz's watch! She yelled something, and the next thing I knew I was breathing again and she asked what kind of music I liked. I said, "Jazz, but I also love club music." She said, "Club music it is," and she ordered the staff (of maybe 30 people) to play club music, then she yelled, "Neffie, you promised me a baby." I was told that I said to her, "You got it," and I bore down and she vacuumed out a beautiful baby girl.

She ordered the anesthesiologist to give me something for the pain but she made me open my eyes to identify my baby.

Then she brought her close to my face and whispered, "You did it." Barely alive and in a weak voice, I said, "*We* did it."

That was a rough night. I was unable to take the medicine that works for cramps and I couldn't see my baby. She was in the neonatal ICU, safe and warm with the best nurses in the world. I was the one in critical condition. When I looked to my left, I had a nurse sitting by my side, and when I looked to my right, the same. I was in such poor condition that I had two critical care nurses sitting two inches away. They told me that the next 24 hours were crucial. My buzzers beeped and alarms went off. The nurses did their jobs and I was right back each time. As soon as I was strong enough – it must have been about 12 hours later – I demanded to see my baby. They made it happen, and what a moment it was. She looked just like my baby picture. She had a tiny IV in her arm and a blood pressure cuff on the other arm. She seemed so content lying there in her own private incubator. I wept thinking about all that she went through.

So days went by and we both got stronger and healthier. Although I did have a minor setback with a bout of pneumonia, I was still able to bring my baby home a week later.

Our journey was just beginning. I was going home to five children and a failing heart. To repair the dissection, doctors had to place three stents in my coronary artery, which required me to take blood thinners and about nine other pills daily. The blood thinners require constant monitoring, especially in the beginning, so I had to travel to Philly every two days with five children while hardly able to walk. It was tough but I was happy to be alive, so I was happy to do it.

About a month later, I found out that my heart wasn't functioning as effectively as they had hoped. I was admitted back into the hospital so that doctors could place a defibrillator into my chest. This is a device used to shock the heart back into rhythm should it stop or begin to beat too fast. Continuing with my positive attitude, I was thankful that such technology existed – several doctors and nurses called me the most positive patient ever!

Nefertari surrounded. Clockwise from the bottom: Shayna (4), Shawna (7), Octavia (19), Olivia (12), and Shawn Jr. (10).

I live today as a disabled person. Although my ejection fraction (a scale that doctors use to measure heart function) at one point was 17 percent (meaning that my heart was functioning at 17 percent of its capability), it is now up to 35 percent. It's still critical but a definite improvement.

I enjoy my life. Don't get me wrong. It is a constant battle fighting depression and anger, but I find myself being thankful for every single moment. I no longer see life as a constant struggle but as an opportunity to make a difference. I know how it feels to be at the brink of death and I am able to tell other heart patients that no matter how bad things may look now, it will get better. I tell them to trust in whatever higher power they believe in and to accept that the future is not in their control. What shall be, will be – so enjoy the present. Life is even more precious once you've almost lost it.

Now I can laugh, shop (with assistance), and drive, and I am almost able to do 45 seconds of dancing to Beyoncé's "Single Ladies"! I have learned to appreciate my medicine and value my doctors. I view the tests and appointments as opportunities to learn more about my condition so I can share with others. I try to remain positive and I smile when I look at my defibrillator scar. I think about how awesome it is that such technology exists. To live in a country that allows someone like me – a middle-class mother of five – to receive such wonderful medical care is just amazing. I'll never take it for granted. ●

Nefertari Nelson-Williams is a freelance writer, an advocate for heart health, and a blogger on heart disease for Healthline.com. Her website is www.nefertarinelson.com.

# A DAY CAPTURED IN PHOTOGRAPHS

*By Daniel Burke*

As part of a university-wide initiative, Daniel Burke turned his camera on many different sites and many different people on April 14. Along the way, he captured nurses arriving for work in the early morning, an ER team conferring, a technician monitoring sleep studies, medical students studying, and surgeons operating, all part of a typical day in the life of Penn Medicine.

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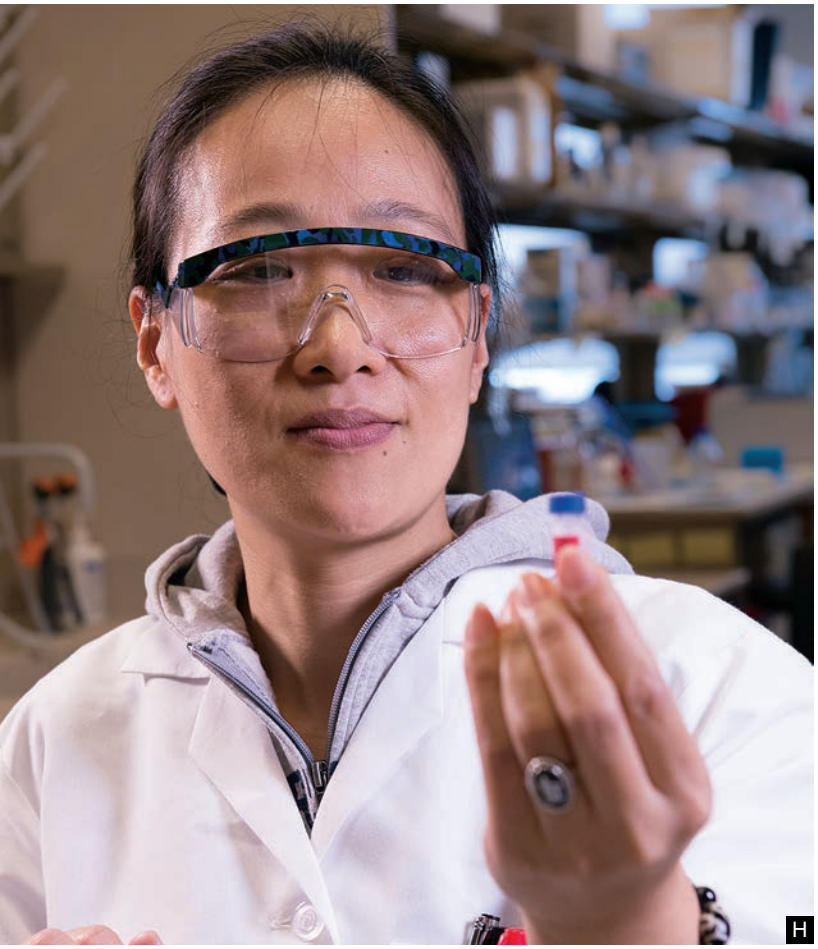

H

**A** 6:00 a.m. Penn Medicine faculty and staff members stream out of the University City SEPTA station.

**B** 7:00 a.m. Nurses grab some portable refreshments as they head to their shifts in the Hospital of the University of Pennsylvania.

**C** 7:30 a.m. Members of the cardiology faculty, residents, and medical students listen to a visiting expert at grand rounds in the Translational Research Center.

**D** 8:30 a.m. Dionne Beadle, a cardiac surgical technologist at HUP, organizes the surgical equipment during a minimally invasive procedure to repair a mitral valve.

**E** 9:00 a.m. Head and neck surgeons perform a sinus operation at HUP.

**F** Ready for use: instruments for the operating room.

**G** 10:00 a.m. Angela Kutchera, a HUP perfusionist, monitors a cardiac procedure.

**H** 11:30 a.m. Helen Gou, a mass spectrometrist in the laboratory of Garret FitzGerald, M.D., in the Translational Research Center, checks for air bubbles in an injection vial to assure that an accurate sample volume will be used in the mass spectrometer.


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SILENT KNIGHT


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I 1:00 p.m. Oluwagbemiga Adeleye, a pharmacy technician, refills medications and supplies throughout the day at HUP. During a typical eight-hour shift, each tech will deliver anywhere from 150 to 250 medications to various floors in the hospital.

J 3:15 p.m. Nova Panebianco, M.D., M.P.H., assistant professor of emergency medicine, far left, leads a discussion about patients at the start of a shift in HUP's emergency department.

K 4:00 p.m. Tamara Bockow, then a fourth-year medical student, teaches a class for the Pipeline Neuroscience Program of the Perelman School of Medicine. The program seeks to interest underrepresented minorities in medical school.

L 5:00 p.m. First-year students study together in Stemmler Hall, preparing for an exam the next day. From left to right: Tarik Asmerom, Christine Bui, and Doug Worrall.

M 7:00 p.m. Dennis Burns, a member of HUP's facilities team for more than 20 years, repairs a broken light.

N 11:30 p.m. Chris Neal, a technician in the Penn Medicine Sleep Center's Overnight Sleep Lab, monitors a patient's vital signs during a sleep study. The technicians will continuously monitor each patient's vital signs until 7:00 a.m.

O HUP ambulances are ready to go at any time of night.

# In the Thick of Things: Jonathan Moreno

*By John Shea*

In his newest book, the Penn Integrates Knowledge professor ranges across disciplines to examine America's longstanding ambivalence toward science.

Science: Americans have long had a love-hate relationship with it. Some Americans have been suspicious of science, its fruits, and its practitioners; others have sung its praises with enthusiasm; and still others have felt an uncomfortable ambivalence. That's the topic of the latest book by Jonathan D. Moreno, Ph.D., *The Body Politic: The Battle Over Science in America* (2011). Moreno is one of the University's Penn Integrates Knowledge professors, 14 at last count, each with academic appointments in two schools. Moreno is a member of the Department of Medical Ethics and Health Policy in the Perelman School of Medicine and of the Department of History and Sociology of Science in the School of Arts & Sciences. With his wide range of interests and expertise, Moreno is well suited to explore the particular strain of American history that is the subject of *The Body Politic*.

The Founding Fathers included several of the most prominent scientists and science-minded men of that time. Thomas Jefferson and Benjamin Franklin are among the most widely known. Less well known, as Moreno points out, are the related ideas of Alexander Hamilton. He proposed prizes, patents, and "premiums" for innovation, "similar to today's tax credits for research and development" (*TBP*, p. 37). One of the epigrams Moreno selected for the book comes from Franklin himself, in a 1780 letter to Joseph Priestley, part of which reads:

"This rapid Progress true Science now makes, occasions my regretting sometimes that I was born so soon. It is impossible to imagine the Height to which may be carried, in a thousand years, the Power of Man over Matter. . . . [A]ll Diseases may by sure means be prevented or cured, . . ."

Even if Science and its companion Medicine have not yet cured or prevented all diseases, it's likely that today's physician-scientists share Franklin's positive vision.

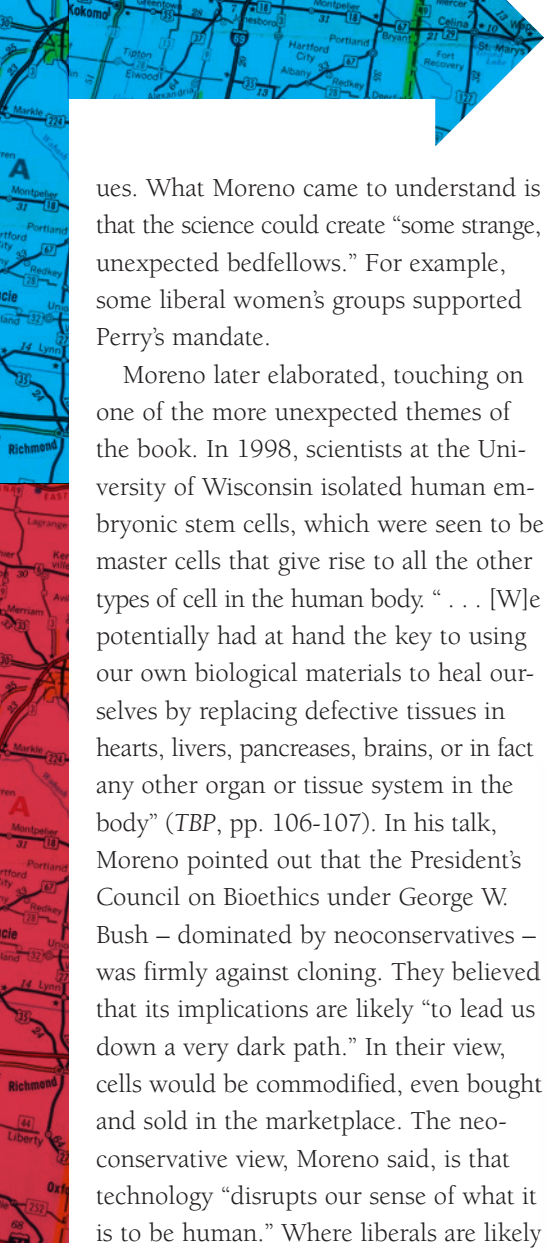
But the second epigram, Edgar Allan Poe's "Sonnet – to Science" (1829), presents a much less favorable view of science. Here it is a vulture that preys on the poet's heart and whose wings "are dull realities." In Poe's view, Science has done little more than drive myth and fantasy away and leave little of worth behind. As Moreno noted in an appearance at the University of Pennsylvania bookstore last fall, Poe's era was also the era of Mary Shelley's *Frankenstein*. Although there is a "monster" in the novel, it is actually Victor Frankenstein, the scientist, who is the villain, a victim of misguided hubris.

In part, this extreme divergence in the views of Franklin and Poe can be explained by the change in the nation's status – from


a brand-new democracy moving forth with enthusiasm and idealism to one struggling with the hard realities of nationhood. But a comparable divergence has been with us to this day. According to Moreno, "Reservations about rapid technological change are widely shared regardless of political party or philosophy. In America the tension between approval of science and worry about the rapid changes it can bring bubbles up in special ways when moral or cultural choices seem to be involved. We've seen this tension play out time and again in our seemingly endless controversies about the teaching of evolution, reproductive rights, the moral status of the human embryo, the origins of the universe, and nearly all the issues of science that relate to human values" (*TBP*, p. 16).

In recent decades, Moreno argues, this division has been sharpened and made more vehement. Today, even politicians feel compelled to state their positions on these divisive issues. Moreno notes that chimeras (organisms composed of two or more genetically distinct cells) have been used in important medical research for decades; pigskin grafts have been used to minimize scarring in humans with severe burns, and cow arterial grafts have been used for reconstructing human arteries. But many people are concerned about future steps. For example, Christine O'Donnell, later to be the Republican candidate for the U.S. Senate in Delaware, appeared on *The O'Reilly Factor* (Fox News) in 2007 as part of a debate on stem cell research. There, she asserted – falsely – that "American scientific companies are cross-breeding humans and animals and coming up with mice with fully functioning human brains." Similarly, in 2009, Gov. Bobby Jindal (Louisiana) signed into law a bill prohibiting human-nonhuman hybrids.

At the Penn bookstore, Moreno described *The Body Politic* as an attempt to gauge the importance of the debates on medical and scientific issues and to put them in a historical and cultural context. Biology, he explained, has become part of national politics – in short, *biopolitics*. One instance involved two politicians then running for the Republican nomination for president, U.S. Representative Michele Bachman (Minnesota) and Gov. Rick Perry (Texas). They squared off about whether the government – of the State of Texas, in this case – should mandate that girls receive the HPV vaccine. The twist in this case was that, on many other issues, Bachman and Perry shared very conservative val-



ues. What Moreno came to understand is that the science could create "some strange, unexpected bedfellows." For example, some liberal women's groups supported Perry's mandate.

Moreno later elaborated, touching on one of the more unexpected themes of the book. In 1998, scientists at the University of Wisconsin isolated human embryonic stem cells, which were seen to be master cells that give rise to all the other types of cell in the human body. " . . . [W]e potentially had at hand the key to using our own biological materials to heal ourselves by replacing defective tissues in hearts, livers, pancreases, brains, or in fact any other organ or tissue system in the body" (*TBP*, pp. 106-107). In his talk, Moreno pointed out that the President's Council on Bioethics under George W. Bush – dominated by neoconservatives – was firmly against cloning. They believed that its implications are likely "to lead us down a very dark path." In their view, cells would be commodified, even bought and sold in the marketplace. The neoconservative view, Moreno said, is that technology "disrupts our sense of what it is to be human." Where liberals are likely to say that embryos are not persons, conservatives insist that embryos are human, not merely "a bag of cells."

The irony, as Moreno explains, is that Marx and Engels made a similar argument about capitalism, that it turns humans and everything around them into commodities. In broad terms, while bioconservatives on the right worry about the implications of extreme capitalism, "green" progressives worry that new technology would increase social inequalities and harm the ecology. Both groups are against science without controls and regulations.

But why on earth would any right-thinking American citizen regard science and scientists with distrust? In *Undue Risk: Secret State Experiments on Humans* (1999), Moreno provided several reasons. In *The Body Politic*, Moreno offers several more. Among the most compelling is the support among some scientists and government officials for eugenics and social engineering. Moreno notes the "Model Eugenical Sterilization Law" published by Harry Laughlin of the Eugenics Records Office at Cold Spring Harbor Laboratory. Laughlin had a doctorate in cytology/cell biology from Princeton University. Some readers will be startled to read the quotation from Oliver Wendell Holmes when, in 1927, the Supreme Court justice wrote a decision upholding a Virginia law. The state invoked the law to sterilize a "feeble-minded" and sexually promiscuous 17-year-old girl.

**"Science is no respecter of the preferences of the powerful. It challenges prejudices, obscures boundaries, and undermines familiar categories. It threatens comforting and stultifying dogma."**

In more general terms, many Americans have felt uneasy about science because it can be seen as subversive. As Moreno puts it, "Science is no respecter of the preferences of the powerful. It challenges prejudices, obscures boundaries, and undermines familiar categories. It threatens comforting and stultifying dogma" (*TBP*, p. 31). The theory of evolution, Moreno notes in the same chapter, upsets a conservative world view and casts doubt on the notion of a designed universe – and the place of humans in it.

In 2010, the National Science Board reported that 68 percent of Americans said that the benefits of scientific research strongly outweigh the harmful results, whereas 10 percent said that the harms outweigh the benefits. But the Board also found that "nearly half of Americans believe that 'science makes our way of life change too fast'" (*TBP*, p. 15). That ambivalence will likely intensify as specialized science becomes more difficult to understand – and when the new biology continues to break down familiar boundaries.

Even if, as Moreno states, science can be disconfirmed by experiment and is a self-correcting process, that may not be comfort enough for many Americans.

Moreno was recruited to Penn in 2006 from the University of Virginia, where he was a professor of biomedical ethics and director of the Center for Biomedical Ethics. He was also a senior fellow at the Center for American Progress in Washington, D.C., a position he retains. The Penn Integrates Knowledge initiative, launched a year earlier by Amy Gutmann, Ph.D., the University's president, seeks to recruit exceptional faculty members whose research and teaching exemplify the integration of knowledge across disciplines. Moreno earned his doctorate in philosophy from Washington University in St. Louis. He also holds an endowed chair, as all PIK professors do: the David and Lyn Silfen University Professorship.

Moreno came to Penn as a highly sought commentator for such TV and radio programs as ABC *World News Tonight* and NPR's *All Things Considered*, and he was frequently quoted in major newspapers and magazines. In his time as a PIK professor, he has not slowed his pace. He has appeared in *The Atlantic* and is a regular contributor to *The Huffington Post*, where he can respond in a timely fashion to many of the events and opinions of the day. More recently, he has also been posting for *Psychology Today*.

Speaking about *The Body Politic* on the Penn campus, Moreno noted that his publisher encouraged him to have a Facebook

page, and he has also has a Twitter account. As he mentioned in an interview, "It is different now. You have to be aware of social media. And I want my ideas out, I want to be 'on the radar.'" In short, Moreno relishes the role of public intellectual, a breed that seemed in danger of extinction.

Topics of his recent postings have included the firestorm over Plan B (also known as the "morning-after pill"), in which Moreno notes that Kathleen Sebelius, Secretary of the Department of Health and Human Services, overruled the recommendations of the Food and Drug Administration and its panel of scientists and denied over-the-counter access to the pill by girls under 17; the widely differing views of what constitutes "personhood" and recent efforts by some conservatives to define it as including the embryo at the moment of conception; and the importance of a "frontier" in inspiring American progress and the possibility that a NASA manned mission to Mars might "save" American science from American politics.

Another recent post by Moreno appeared first in *The Wall Street Journal*: "Robot Soldiers Will Be a Reality – and a Threat." In the piece, he cites technologies "on the horizon," including using brain-machine interface technologies to give remote pilots of drone aircrafts instantaneous control through their thoughts alone. Another technology being explored is "whole brain emulation," which would involve "uploading a mind from a brain into a non-biological substrate." But what might advantage one side in a conflict would likely be turned against it in time. Moreno concludes that "fully autonomous offensive lethal weapons should never be permitted."

In *Mind Wars: Brain Science and National Defense* (2006) and elsewhere, Moreno has made similar points – that technologies that derive in some way from defense-funded projects are often open to dual use. They can be used for the general good as well as in military situations, and discoveries in neuroscience can be adapted for military use. As he said in an interview with *Science & The City* (2006), " . . . there's evidence that beta blockers, which are used for people with heart disease, can be used to treat people with post-traumatic stress disorder. There are some people who believe that not only are they useful after someone has been in a stressful situation, but it might even be plausible to give somebody a beta blocker before they go into a stressful situation. . . . Imagine if you were to give a beta blocker to a soldier before he or she went into a combat situation. On the one hand you might prevent or at least ameliorate the terrible emotional feelings that could come from what they see and do in combat, but, to put it in a single phrase, do we want an army of guilt-free soldiers"?

Another point that Moreno emphasized in *Mind Wars* is the responsibility of scientists to consider the social and ethical issues raised by their research. While writing the book, he could not persuade many neuroscientists "to talk for the record about the downside of their own field's involvement in national security work" (*MW*, p. 5).

Moreno has a distinguished record of service on several important commissions that have influenced public policy. These include the National Human Research Protections Advisory Committee, the National Bioethics Advisory Commission, and the President's Committee on Human Radiation Experiments. An elected member of the Institute of Medicine of the National Academies, Moreno was co-chair of the Committee on Guidelines for Human Embryonic Stem Cell Research, sponsored by the Institute of Medicine and the National Research Council. He has also served as president of the American Society for Bioethics and Humanities.

It is not surprising that the career arc of such a visible bioethicist would have intersected with Penn's prominent Center for Bioethics. In 1998, when the Human Research Ethics Group published its report in *The Journal of the American Medical Association* on updating protections for human subjects involved in research, Moreno was lead author. The Human Research Ethics Group as a whole was administered by

## What Is Biopolitics

Biopolitics is the nonviolent struggle for control over actual and imagined achievements of the new biology and the new world it symbolizes. Whether that world is seen as better or worse than our own, the very idea of such power stimulates deep reservations on both the left and the right about the implications of the post-Enlightenment, scientific worldview. . . . But when the full range of biopolitical issues are considered along with the motivating concerns behind them, the picture turns out to be far more complicated than is captured by the left-right spectrum. Consider, for example, those who might broadly be identified as bioconservatives: they worry that the life sciences will modify human abilities in comparison with some natural norm. But there are bioconservatives on the right and on the left. Bioconservatives on the right emphasize that a loss of traditional values could result, especially the dignity that should be ascribed to all persons. Bioconservatives on the left focus on the possibility that social inequalities and ecological problems could be grievously aggravated by biotechnological innovations.

(*The Body Politic*, p. 121)


Penn's Center for Bioethics and included such Penn authors as Arthur L. Caplan, Ph.D., founding director of the center, who will soon be concluding his 18-year stay at Penn and moving to N.Y.U.'s Langone Medical Center, and Paul Root Wolpe, Ph.D., who now heads the Bioethics Center at Emory University. (Caplan and Moreno, in fact, knew each other as graduate students in New York City in the 1970s.)

About Moreno, Caplan says, "Jonathan has an unmatched ability to use history to illuminate current debates in bioethics. He brings a broad vision to his work and is able to incorporate an understanding of cutting-edge science into his incisive, historically grounded, normative thinking."

In the midst of the more recent theoretical and historical books that Moreno has written or edited, *Ethics in Clinical Practice* seems something of an anomaly. The second edition, written with Judith C. Ahronheim, M.D., and Connie Zuckerman, J.D., appeared in 2005. As the preface puts it, this edition "gives heightened attention to newer ethical dilemmas spawned by the advances in medical genetics, organ transplantation, HIV medicine, and assisted reproductive technologies, and by complementary/alternative medicine, managed care, physician-assisted suicide, and other timely issues." In effect, the second edition of *Ethics in Clinical Practice* illuminates many of the issues that underlie *The Body Politic*, but from a different angle. Or a combination of angles, given that the book was "prepared collaboratively by a physician, a philosopher, and an attorney. . . ." Here the focus is on everyday practice, not from a distance but on the ground level. After some general discussion, the authors look closely at 31 hypothetical – but realistic – cases. Among them: "Withholding Tube Feeding in a Woman with Advanced Dementia"; "'Do Everything': Physician Obligations in the Face of Family Demands"; and "A Pregnant Woman Using Cocaine." In each case, the primary issues to consider are named, followed by fuller medical considerations, and then ethical and legal considerations.

Confronting such issues was in some ways Moreno's introduction to bioethics. He was a young professor of philosophy when the call came to teach a new course in bioethics. As Moreno puts it, an untenured assistant professor never says no in such situations! He would teach Philosophy 101 in the morning to 80 undergraduates "who were barely there"; then, in the afternoon, he would talk with physicians "who were hanging on my every word" as they considered the issues they had to face at the university's hospital. Those situations were often tense, often tangled – precisely like those described in *Ethics in Clinical Practice*.

For about 20 years, Moreno focused on clinical ethics. What precipitated his shift to a different kind of ethics was being appointed to the President's Committee on Human Radiation Experiments. He came to realize that bioethics could play an important role in shaping public policy. From there it was a short step to considering the ethical aspects of such important issues as national security and neuroscience. "You can understand so much through the nation's security concerns," he says. When *Undue Risk* appeared in 1999, *The New York Times Book Review* noted that "the historical record he presents in *Undue Risk* strongly supports his contention that the rights of human subjects deserve to be held paramount over any needs of national security."

Only two years later, a different kind of security concern struck the United States: the anthrax attacks. Moreno realized that there was nothing in the bioethics literature about biological weapons. In addition, even as neuroscience was burgeoning, nobody was exploring the national security angle. "I was afraid some smart science writer was going to write it first," he says. But he published *Mind Wars* in 2006, to very favorable reviews. Again, the critics praised his clear, conversational prose. And, despite his affiliation with the liberal-leaning Center for American Progress, his moderate, balanced tone.

From his affiliation with the Center for American Progress, it's clear that Moreno considers himself a progressive. At a campus Knowledge by the Slice presentation this spring, he stated, "I leave my politics at the classroom door," but he feels freer to express those views in his writing. Still, Moreno clearly intends to avoid the noisy back-and-forth assaults parodied in the early days of *Saturday Night Live*. In *The Body Politic*, he discusses a neoconservative writer's criticism of "the new commerce of the body" – paid egg donations, the market in medications for erectile dysfunction, and so on. The writer blames technology and cultural permissiveness, with no mention of the underlying socioeconomic forces. Moreno answers: "One would think the blame for these problems lies partly with an economic system that allows everything to be priced and sold."

His approach is more in line with what the Center for American Progress urges on its Web site: "Challenge conservative misinformation with the facts." Heat not necessary. In fact, in an interview, Moreno points out that some of the harshest criticism of *The Body Politic* has come from the left. That kind of response, he says, "helped me understand how it was so easy to fall into the conventional scheme." He recalls what a good teacher said: "Give me the best argument you can *against* your position." A student's position will stand or fall depending on how it withstands such scrutiny.

Moreno's father, J. L. Moreno, was a well-known psychiatrist, born in Austria, who is considered the pioneer of group psychology, role playing, psychodrama, and encounter groups. His mother, Zerka T. Moreno, is a psychotherapist. (She has just published a memoir at the age of 94.) They had a private 20-acre sanitarium in New York's Hudson Valley. When I suggested that the young Moreno's household and upbringing were not at all like those depicted in the typical situation comedies of the late 1950s and early 1960s, he laughed. "In some respects, it was very close to *Leave It to Beaver*." His childhood home, he continued, was picturesque Americana but depressed, something of "a shabby river town."

But there were certainly some telling differences from the old sitcom. At the beginning of *Mind Wars*, Moreno recounts an episode that he did not understand at the time. One Saturday morning, a yellow school bus arrived at the sanitarium and dropped off about two dozen young men and women. Ten-year-old Jonathan organized an impromptu softball game with them, and they played for an hour. Then the visitors went inside. "Years later, when I was a college student, I asked my mother, who worked closely with my father, about that weekend. 'Oh,' she said, 'that was a group of patients referred to your father by a psychiatrist in Manhattan. They were here to try LSD as part of their therapy. It didn't work.'" At the time, the senior Moreno was authorized to order certain controlled substances from government-approved producers for his work. For Moreno, the episode was an unsuspected exposure to some later concerns like bioethics and neuroscience.

**"In America the tension between approval of science and worry about the rapid changes it can bring bubbles up in special ways when moral or cultural choices seem to be involved."**

Given his wide interests, I asked Moreno what he brings to his work and at what stage: philosophy, American history, bioethics? "I can't disentangle them anymore," he replied, calling himself "disconcertingly interdisciplinary." He is, he confessed, "interested in everything – thank God for PIK!" Moreno drew a contrast to his father's era, when the barriers between disciplines were not so strong. The senior Moreno pursued psychiatry, theater, theology, and whatever else interested him. It is a pattern Jonathan seems to have embraced as well.

Which may be one reason he hesitated when asked what he likes to do when not engaged in his work. "I'm pathetic," he replied with a grin. He goes to dinner, goes to the gym, travels. Then he mentioned one pastime that is not at all surprising – reading. At the recommendation of a friend, he reread *Enders Game*, a science-fiction novel by Orson Scott Card. He was currently reading *Plain Honest Men: The Making of the American Constitution* (2009), to try to understand the Founding Fathers more. The author, Richard Beeman, Ph.D., is a longtime professor of history at Penn and former associate dean of the School of Arts and Sciences. Another book that is holding Moreno's interest is the fourth volume in Robert Caro's monumental biography of Lyndon Johnson.

For Moreno, history appears to be a constant. Perhaps it offers some comfort as well. After all, in *The Body Politic*, he suggests that America is a product of the Enlightenment. "It is fair to say that no nation has ever been founded by people who were more oriented toward the pursuit and propagation of knowledge than the United States" (p. 35). The nation is, in effect, an idea and, to borrow a term from science, an experiment. Moreno has no sympathy for what he calls "a gloating 'American exceptionalism,'" and he acknowledges that America's history "is stained with the blood of those who were left out" (p. 185). But its history as a whole, its progress so far, provide reasons for hope. •

# Development Matters

## PICTURE-PERFECT: MEDICAL


It was a festive scene at Medical Alumni Weekend 2012, with much to celebrate. More than 630 Perelman School of Medicine alumni and their guests returned to campus, and many reunion classes had record attendance and fundraising. Together, the reunion classes raised more than $1.7 million, demonstrating that their commitment to their medical alma mater remains strong. While honoring the past, events at Medical Alumni Weekend also spoke of the future, from new classrooms for current Perelman School of Medicine students to a new center for research and treatment of BRCA-related cancers. The weekend wrapped up with Commencement, featuring Dr. Peter Agre, Nobel laureate and former president of the American Association for the Advancement of Science.

**Walter Gamble, M.D. '57, and Anne Gamble were honored with the Lifetime Achievement Award** at this year's Medical Alumni Weekend. The largest alumni donors to the Raymond and Ruth Perelman School of Medicine, their dedication and compassionate philanthropy is allowing generations of new physicians to benefit from a Penn education. They also make it a point to get to know all of the scholarship recipients they support – celebrating their students' life milestones as though they are family. "The real impact of the Gamble Scholars program is not measured in the number of dollars," explained Dean Jameson, "but in the number of stories that the program has made possible."

This year's **Dean's Dinner festivities** were held at The Franklin Institute, highlighting the historical link to Ben Franklin's university as well as the promise medicine holds for the future. "What has struck me most during my first Medical Alumni Weekend," Dean Larry Jameson shared with the 200 assembled alumni and guests, "has been witnessing your passion for the School and your dedication to our students. Your drive to maintain our rich tradition in training future generations of physicians both inspires and invigorates me."

Faculty and alumni alike were excited to hear from G. Michael Lemole Jr., M.D. '95, the neurosurgeon who cared for former **Congresswoman Gabriel Giffords** following an assassination attempt in January 2011. "Gabby deserves a tremendous amount of credit for her remarkable recovery," said Dr. Lemole. "I am proud to say that I was able to help get her on that road thanks to my world-class training at Penn."

# ALUMNI WEEKEND 2012

The Class of 1962 carried on its tradition of gathering at the Jordan family home – thanks to hostess and Reunion Committee Member, Barrie, widow of the late Henry Jordan, M.D. '62 – during its **50th reunion weekend**. Dean Jameson and former dean Arthur Rubenstein, M.B.,B.Ch., also joined the celebration. As Dr. Rubenstein noted, "It is so important to renew cherished relationships and bonds with old friends and classmates."

The **reunion classes "let the good times roll"** across the City of Philadelphia. Members of the Class of 1982 reenacted their "SPOOF" sketch during their dinner at the Hyatt at the Bellevue, capping off a record-breaking attendance and fundraising effort for the 30th Reunion.

Young alumni from the Classes of 2002 and 2007 also enjoyed a lively evening at Graffiti Bar.


The Abramson Cancer Center heralded the creation of the **Basser Research Center for BRCA** during a session called "Meet Penn's Game Changers in Cancer – How Science is Accelerating Cancer Therapy." Mindy Basser Gray, C '92, and her husband Jon Gray, C '92, W '92, made the $25 million gift that launched the Center. "As Penn graduates," they said, "we are fortunate that our alma mater has the world-class medical facilities and gifted researchers essential to helping eliminate BRCA-related cancers."

Returning alumni were invited to go back to school in the **new classrooms in Stemmler Hall** during "From Microscopes to Microchips: Medical Education in the 21st Century." Featuring both leading-edge technology and flexible work spaces, the classrooms allowed alumni to have a hands-on experience on how medical students are trained today.

Nearly seven tons of fixtures and furnishings removed from Stemmler during the renovation are in the classroom again. Thanks to a partnership with the Recycling Network and Corporate Interiors, these materials were donated to the Enrique de Osso School in Nicaragua, which supports more than 1,300 students.

## Progress Notes

*Send your progress notes to:*
Donor Relations
*Penn Medicine Development and Alumni Relations*
*3535 Market Street, Suite 750*
*Philadelphia, PA 19104-3309*

# '50s

**David E. Kuhl**, M.D. '55, G.M. '59, a former professor of radiology at the University of Pennsylvania, the University of California Los Angeles, and the University of Michigan, received the John Scott Award in November. Nominations for the award are made by a committee of Philadelphians to the Board of Directors of City Trusts of the City of Philadelphia. Dating back to 1834, the award is given to the "most deserving" men and women whose inventions have contributed in some outstanding way to the "comfort, welfare, and happiness" of mankind.

Kuhl was recognized for a scientific discovery that opened up a whole new way of examining cellular metabolism in the human body – Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET). Today, these two imaging techniques are used in a majority of hospitals around the world and allow diagnosticians and clinicians to visualize cross-sectional imaging of patients by using radioactive tracers. According to Kuhl, "This has been an evolution which involved many people. It's all very exciting because PET offers better data, extraordinary chemistry, and better pictures. Not only does it enable physicians to see into the body, this diagnostic imaging shows the metabolic and neurochemical processes as well."

Prior honorees include Christian J. Lambertsen, M.D. '43 (2010), the late founder of Penn's Institute for Environmental Medicine, for his invention of the underwater breathing apparatus known as SCUBA; Jonas E. Salk (1954), for discovering the Salk poliomyelitis vaccine; and Sir Alexander Fleming (1944), for his discovery of penicillin.

# '70s

**Robert L. Barchi**, Ph.D. '72, M.D. '73, who has served as president of Thomas Jefferson University since 2004, has been named the 20th president of Rutgers, The State University of New Jersey. Barchi began his academic career as a faculty member at the University of Pennsylvania in 1972, rising to become the David Mahoney Professor of Neurological Sciences. He was also director of the David Mahoney Institute of Neurological Sciences, founding chair of the Department of Neuroscience, and chair of the Department of Neurology.

In 1999, he was named provost of the University of Pennsylvania, its chief academic officer. In this role, Barchi had responsibility for the University's 12 schools and their academic programs and budgets, as well as for Penn's students and faculty. During his tenure, he established a number of University-wide interdisciplinary educational and research institutes.

Under his leadership as president of president of Thomas Jefferson University, the University grew from three to six schools and enrollment across the campus increased by 51 percent. Despite the economic downturn, fundraising has more than doubled.

For more than 30 years, Barchi headed a research laboratory that was awarded continuous funding by the National Institutes of Health, and he is widely respected for his pioneering work on the structure and function of voltage-gated ion channels and on the role these important molecules play in human disease. In 1993, he was elected to the Institute of Medicine of the National Academy of Sciences. A fellow of the American Association for the Advancement of Science, the American Neurological Association, and the American Academy of Neurology, Barchi has also been elected to the American Society for Clinical Investigation and the Association of American Physicians.

# '80s

**Howard Frumkin**, M.D '81, G.M.E. '85, M.P.H., Dr.P.H., is an editor of *Making Healthy Places: Designing and Building for Health, Well-being, and Sustainability*, published in 2011 by Island Press. According to the publisher, the book clarifies "a pressing need to create healthy places and to reduce the health threats inherent in places already built." Frumkin is dean of the University of Washington School of Public Health and a professor of environmental and occupational health sciences there. From 2005 to 2010, he held leadership roles at the U.S. Centers for Disease Control and Prevention, most recently as special assistant to the CDC Director for Climate Change and Health.

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## OBITUARIES

# '30s

**Homer B. Fegley**, M.D., G.M.'36, Topton, Pa.; December 14, 2011. He served as a captain in the U.S. Army with the 110th anti-aircraft battalion during World War II from the invasion of Omaha Beach until his discharge in 1946. He received five battle stars and the Legion of Merit Medal for exceptional duty. Fegley was one of the founding doctors of Gnaden Huetten Hospital, in Lehighton, where he served as chief of obstetrics and gynecology and associate chief of surgery. In 1968, he was invited to assist in opening the Emergency Department at the Danbury Hospital, Conn. A charter member of the American College of Emergency Physicians, he retired from Danbury Hospital in 1976.

# '40s

**Ferdinand G. Weisbrod**, M.D. '42, G.M. '50, Springfield, N.J., a gastroenterologist for more than 30 years at East Orange General Hospital; September 20, 2011. During World War II, he served with the U.S. Army Air Corps in Europe. After retiring from medicine, he founded Forest Realty, Inc. His brother was Lawrence M. Weisbrod, M.D., G.M.E. '48, an orthopaedic surgeon.

**David B. Coursin**, M.D. '43, G.M.E. '47, Madison, Wis., a consultant pediatrician; July 22, 2011. He established the pediatrics department and research institute at St. Joseph's Hospital. An editor of *Nutritional Support of Medical Practice* (1977, 1983), he had served on the editorial board of *The Journal of Nutrition*. He chaired the Subcommittee on Nutrition, Brain Development, and Behavior of the Committee on International Nutrition Programs, which issued a report in 1973.

**Rheim M. Jones**, M.D. '43, Idaho Falls, Idaho, a retired ophthalmologist; May 18, 2010. He was a diplomate of the American Board of Ophthalmology and a Fellow of the American College of Physicians and had been a senior surgeon in the U.S. Public Health Service. A Mormon, he served in many positions, including bishop, regional representative of the Twelve, and president of the Idaho Falls Temple, 1984–87.

**Horace T. Lavely Jr.**, M.D. '43, Nashville, a retired assistant clinical professor of gynecology at Vanderbilt University; October 7, 2011. He entered the U.S. Army Medical Corps in January 1944, serving as a battalion surgeon with three airborne divisions; he received a Bronze Star and was discharged as a major.

**William J. MacMurtrie Jr.**, M.D. '43, Ardmore, Pa., a retired surgeon; November 13, 2011. He was in the Navy at Bethesda Naval Hospital during and after World War II. In 1950 he joined Mercy Fitzgerald Hospital in Darby. From 1981 to 1986, MacMurtrie was vice president of medical affairs for Mercy Catholic Medical Center, which included Mercy Fitzgerald Hospital and Mercy Hospital in Southwest Philadelphia. He was a surgeon at both hospitals and maintained an office in Upper Darby and later in Drexel Hill. He also was an associate professor of surgery at Thomas Jefferson Medical Center. MacMurtrie was a board member of the Academy of Natural Sciences and of St. John Vianney Hospital in Downingtown. He also served on the President's Council of St. Joseph's University.

**R. Robert Tyson**, M.D. '44, G.M.E. '48, Worcester Township, Pa.; November 6, 2011. After serving in the U. S. Navy from 1946 to 1948, he joined Temple University Medical School as an instructor in sur-

gery in 1952. In 1962, he was named a full professor at the medical school and chief of the vascular surgery section at the hospital. He was chief of surgery there from 1973 to 1983, and he chaired Temple's professional advisory committee in 1975. He had served as president of the Philadelphia County Medical Society and the Pennsylvania Medical Society and was chair of the board of Pennsylvania Blue Shield from 1988 to 1992. Author of 78 scientific articles and five films about vascular surgery, Tyson was a Fellow of the College of Physicians of Philadelphia and of the Philadelphia Academy of Surgery.

**John Carpenter Sonne**, M.D. '49, G.M.E. '50, G.M.E.'52, Galena, Md., a retired psychoanalyst; November 12, 2011. He had served in the U.S. Navy. A pioneering researcher and clinician, Sonne held several academic posts. As an analyst and therapist, he had a long-standing interest in family dynamics and in prenatal life. His scholarly works and talks advanced the understanding of the effects of abortion on both the unconscious and family health. In one article, he argued that the murderous actions of tyrants can be explained as symptoms of abortion survivors deriving from trauma during prenatal life. He was the author of *A Primer for Family Therapists* (The Thursday Press, 1973). Sonne was a Distinguished Life Fellow of the Pennsylvania Psychiatric Society, and he had served as a class agent for the Class of 1949.

# '50s

**John A. Koltes Jr.**, M.D., G.M.E. '51, Philadelphia, a psychiatrist for Chestnut Hill Hospital; September 29, 2011. He was the first director of the psychiatric unit of Thomas Jefferson Hospital. During World War II, he joined the U.S. Army, and in 1950, he re-enlisted in the Army Medical Corps.

**William H. Wilkinson**, M.D. '52, G.M.'56, formerly of Devon, Pa.; January 9, 2011. He served in the U.S. Army as a sergeant during World War II and a second time in the U.S. Air Force as a captain and flight surgeon and was a senior assistant surgeon during the Korean conflict. Wilkinson retired from Merck Pharmaceutical Company.

**Arthur F. Calnan**, M.D., G.M. '54, Scituate, Mass., a retired ophthalmologist; October 20, 2011. He was a captain in the U.S. Air Force Medical Corps during the Korean War, serving as a Flight Surgeon. He established his own private medical practice in 1971 and was on staff at South Shore Hospital for 32 years. In addition, he founded the Eye Department at Lahey Clinic in Boston and was on staff at Massachusetts General and Massachusetts Eye and Ear.

**James F. O'Rourke**, M.D., G.M. '54, Farmington, Conn.; October 29, 2011. He was in the U.S. Navy during World War II. From 1955 to 1957, he was chief of clinical research at the National Institutes of Health's ophthalmology branch, and he served as professor of surgery in ophthalmology at Georgetown Medical School 1958-69. At Georgetown, he established the first ophthalmology residency program. In 1969, the University Connecticut recruited O'Rourke for the new health center in Farmington. He became the first director of its ophthalmology division, a position he held until 1988. The author of more than 100 research articles on a wide array of topics, O'Rourke also served as director of the Connecticut Lions Vision Center for nearly 40 years. Subsequent positions included professor of pathology, adjunct professor of surgery, and adjunct professor of engineering at Trinity College in Hartford. O'Rourke's focus was on the tiny capillaries of the retina and how they reflect the health of the whole body. His research achievements included a discovery that tissue plasminogen activator (tPA), the clot-busting protein given to stroke victims, is produced naturally under conditions of stress. In 1994, O'Rourke was presented the Leader of Vision Award by the Connecticut Eye Bank and Research Foundation.

**Capt. Howard A. Baker**, M.D., G.M.E. '55, Bradenton, Fla., a retired surgeon; November 15, 2011. He joined the U.S. Navy in World War II and served as a ship surgeon on the cruiser *U.S.S. Baltimore* (CA-68) and a hospital ship off the coast of Nagasaki after the atomic bomb was dropped. He was recalled from private practice to active duty in the Korean War and later served as executive officer of the U.S. Navy Hospital Guantanamo Bay at the outset of the Cuban Missile Crisis. He was the division surgeon for the Second Marine Division and the force surgeon for the Marine Corps in Vietnam, where he received the Bronze Star for valor. He retired from the Navy as commanding officer of the U.S. Navy Hospital in Corpus Christi, Texas. After returning to private practice, he retired in 1994.

**Waldo R. Fisher**, M.D. '56, Ph.D. '64, Gainesville, Fla.; November 9, 2011. He joined the faculty of the University of Florida in 1965 and held appointments in the departments of Medicine and Biochemistry. When he retired in 2000, he had attained the rank of Distinguished Service Professor of Medicine. Fisher's research focused on structural and metabolic differences of the lipid transporting proteins of human plasma in normal and diseased states of fat metabolism and was instrumental in the development of treatments for high cholesterol. These investigations were funded by the National Institutes of Health for more than 30 years, during which he was also a visiting scientist and consultant at NIH in multiple capacities. In 1996, he received the University's Faculty Research Award in Clinical Science. In 1986, the National Institute of Dyslexia honored him with the Margaret Byrd Rawson Award for his achievements as a dyslexic person. He had also served as president of the Alachua County chapter of the American Cancer Society.

**Thomas J. Cook**, M.D. '59, Norwich, Conn., a retired dermatologist; November 24, 2011. He served as clinical associate professor at Yale University School of Medicine from 1964 to 2001 and was a member of the American Academy of Dermatology.

**Stanley Davis Fons**, M.D. '59, Bedford, N.H.; September 21, 2011. During his many years at Elliot Hospital in Manchester, he served in several capacities, including chief of staff and head of the diagnostic radiology department. He was instrumental in securing the hospital's first CT scanner and also taught in the hospital's radiology technician school. He also served as a major in the New Hampshire National Guard.

**Jamshid Hamed**, M.D., G.M. '59, Towson, Md., a retired internist; November 8, 2011. Born and raised in Uzbekistan, he had been on the staff of the old Baltimore City Hospital in the early 1960s. He then joined the Greater Baltimore Medical Center in Towson. Hamed also maintained a private practice for more than 30 years until retiring in 2000.

**Daniel William Terry**, M.D., G.M. '59, Sacramento; November 1, 2011. He entered the Navy after Pearl Harbor and was stationed on Midway Island before, during, and after the Battle of Midway. He was recalled into the Korean War and was stationed aboard the *U.S.S. General Pope* as the ship's medical officer. A graduate of Creighton University's medical school, he joined the Radiological Associates of Sacramento. He later became chief of radiology at the Sacramento VA Medical Center. A diplomate of the American Board of Radiology, he had been president of the Sacramento Medical Society.

# '60s

**Gordon J. Pentecost Jr.**, M.D., G.M. '60, Troy, N.Y., a retired ophthalmologist who had maintained a practice for 54 years; January 12, 2011.

**Thomas H. Irving**, M.D., G.M.E. '64, Lima, Pa., an anesthesiologist; November 26, 2011. He served with the U.S. Navy and spent most of his professional career at Wake Forest University's Bowman Gray School of Medicine. There, he served as the first chair of the Department of Anesthesiology. After retiring from academic medicine, he entered private practice in Statesville, N.C., and then in Pittsburgh until he retired in 1993.

# '70s

**Eugene A. La Lancette**, Ph.D., M.D. '70, G.M.E. '74, Fitchburg, Mass.; October 19, 2011. He worked as a research chemist at

the DuPont Co. for six years and published numerous articles in professional journals. After earning his medical degree, he moved back to his home town of Fitchburg, where he was in family practice medicine until retiring in 2001. A former president of the medical-dental staff at Burbank Hospital, he was named the Community Clinician of the Year in 2001 by the Massachusetts Medical Society.

**Richard Alan Sollitto**, M.D. '78, San Francisco, a retired radiologist; November 26, 2011. In 1983 he joined the Department of Radiology of the University of California at San Francisco, where he remained for 28 years until his recent retirement as a clinical professor. In that time, he was chief of radiology in the Ambulatory Care Clinics and Mount Zion campuses and associate chair of the Department of Radiology. He was a founding board member and president of the Margulis Society, which supports the training of radiology residents and fellows. Sollitto was also on the board of Community Hospice Foundation of the Bay Area.

## '80s

**Patrick T. Liu**, M.D. '89, Paradise Valley, Ariz., diagnostic radiologist at the Mayo Clinic in Scottsdale; January 25, 2012. A competitive cyclist for almost three decades, he sustained a spinal cord injury while mountain biking and died of pneumonia 18 months later. In 2001, one of his articles was honored as a "Paper Winner" by the Society of Skeletal Radiology, and in 2011, the Society introduced the Patrick T. Liu Innovation in Research Award at its annual meeting. He was married to Margaret Mary Stemmler, M.D. '88, daughter of Edward J. Stemmler, M.D. '60, G.M.E. '64, former dean of Penn's School of Medicine.

## '90s

**Duane Anthony Sewell**, M.D. '94, Baltimore, an associate professor of otorhinolaryngology at the University of Maryland; November 27, 2011. His focus was on cancer immunotherapy research. A former assistant professor at Penn, he also worked as a staff surgeon at the VA Medical Center in Philadelphia. Among his honors were the Outstanding Medical Student from the Medical Society of Eastern Pennsylvania, the Helen O. Dickens Award from the University of Pennsylvania Medical School, and the Percy Memorial Research Award from the American Academy of Otolaryngology. He was married to Catherine A. Pilgrim Sewell, M.D. '94, director of the Johns Hopkins Fibroid Center.

## '00s

**Jagajan Karmacharya**, M.D., G.M. '07, Miami, associate professor of surgery at the University of Miami and chief of vascular surgery at the Miami VA hospital; September 26, 2011. He had earned his medical degree from the University of Calcutta. He was among those killed in a plane crash in his homeland of Nepal.

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FACULTY DEATHS

**Edward J. Resnick**, M.D., Bala Cynwyd, Pa., an instructor in orthopaedic surgery from 1960 to 1964; October 25, 2011. He was chief of orthopaedic surgery at the Philadelphia General Hospital from 1964 to 1967. Later, he was a professor at Temple Medical School. He had served as president of the Philadelphia Orthopaedic Society, the Philadelphia County Medical Society, and the Pennsylvania Orthopaedic Society. From 1978 to 1996, he was a member of the executive committee and board of directors of Pennsylvania Blue Shield.

**Louise Schnaufer**, M.D., Philadelphia, emeritus professor of pediatric surgery; October 14, 2011. She was the first woman chief surgical resident at Union Memorial Hospital in Baltimore. In 1999, she was honored by the American Academy of Pediatrics as an outstanding mentor of trainees in pediatric surgery. The Children's Hospital of Philadelphia established the Louise Schnaufer Endowed Fellowship in Pediatric Surgery in her honor in 1995.

LEGACY GIVING

# For Charles Saunders, Penn Reunions Offer Something New Every Time

*When it comes to attending reunions, Charles Saunders, M.D. '67, G.M.E. '74, has sustained an impressive streak. He has been to every reunion of his medical school class, often volunteering on the Reunion Committee as he did for this year's 45th Reunion celebration. Yet despite his many visits, Dr. Saunders finds something new every time he returns to the Perelman School of Medicine campus.*

*"I am always struck by Penn's superiority to other medical schools," he said. "I watch the new buildings go up, but what makes Penn really stand out is what goes on in those buildings — medical breakthroughs, excellent professors, and eager students."*

*Dr. Saunders and his wife, Sheila Landau Saunders, C.W. '65, G.E.D. '67, were once among those eager students. He went on to a successful career as a urologist and also served as the senior vice president of medical and academic affairs at the St. Luke's University Health Network in Bethlehem, Pa. Now retired, he is currently a trustee for the organization. Mrs. Saunders co-owned Senior Solutions, a geriatric-care management firm.*

*Charles and Sheila Saunders consider Penn a special place, and they have made a gift every year since Dr. Saunders graduated. A few years ago, they discovered something new — the charitable gift annuity, a creative way to give back to Penn through planned giving. Since 2007, they have created three charitable gift annuities benefitting the Medical Class of 1967 Scholarship Fund.*

*"We learned about charitable gift annuities through the Penn Medicine Planned Giving Office, and we are very pleased that we can both honor Penn and help today's students," said Dr. Saunders. "The cost of medical education is extremely high, and students must accumulate large debt. They need help to be able to complete their medical education. In return, we receive payments, and, for a retiree like me, I benefit as well. We all win."*

*With a charitable gift annuity, the donor transfers cash or stock to Penn Medicine and receives a guaranteed lifetime annuity payment and a current income tax deduction. Ultimately, the remaining funds go to the Penn program designated by the donor. It is a mutually beneficial arrangement, and one of the simplest ways to make a gift.*

*Charles and Sheila Saunders chose one of a multitude of creative gift opportunities that benefit both Penn Medicine and donors. As you plan your financial future, the Office of Planned Giving is ready to assist in developing an appropriate strategy to incorporate your charitable objectives. Contact Christine S. Ewan, J.D., senior director of planned giving, at 215-898-9486, or e-mail her at cewan@upenn.edu. For more information, please visit the website at www.plannedgiving.med.upenn.edu.*

## More Than Serendipity

"We were kept in large holding areas surrounded by barbed wire. We had frequent roll calls, were constantly checked for hidden weapons. . . . Life as a prisoner of war was marked by an unsettling boredom. . . . After a time, we were moved by truck through Tunisia and ended up in a camp that I will never forget. We were stripped naked, our belongings were searched, and all valuables confiscated."

It was May 1943, and the writer was probably at his bleakest point. He was an 18-year-old soldier who had been part of Germany's renowned Africa Corps for only about four months. While Field Marshall Erwin Rommel was back in Germany on sick leave, it was a different general who had signed the unconditional surrender to the Allies. Where does one possibly go from here – from being a POW in Africa?

The next step was another major one, but it did not necessarily seem fortunate at first: he was among the German prisoners shipped that summer to the United States. Once there, he and the rest of the prisoners went through a delousing station, where they were stripped and sprayed with DDT. Like the others, he received his POW number (8WG-22939). His prospects seemed dim indeed.

But Karl Rickels was not one to give in to despair. He knew more English than the other prisoners and did his best to improve his language skills. He was a hard worker, no matter what the task, and he was able to make himself a dependable – sometimes indispensable – prisoner. Today, he is an internationally known psychiatrist at the Perelman School of Medicine, considered a pioneer in the field of psychopharmacology. At Penn, he founded the Mood and Anxiety Disorders section of the Department of Psychiatry. In 2008, he received the William Osler Patient-Oriented Research Award, one of the Awards of Excellence that are the highest honors the medical school bestows to its faculty members. In *A Serendipitous Life: From German POW to American Psychiatrist* (Notting Hill Press, 2011), originally written for his grandchildren, he looks back at his long journey.

Rickels makes clear in his first chapter that his family did not support Hitler. In fact, he notes that in 1933, when the Nazi party came to power, it received only 44 percent of the total vote – but that was the largest tally of the several parties involved. In Berlin, where the Rickels family lived, the Nazis took only 22 percent of the vote. When Karl became old enough to be drafted into the war, his father advised him to enlist to fight in Africa. The senior Rickels was certain Germany would lose the war, and it would be far better to become a prisoner of war of the British rather than of the Russians.

## Psychiatry at a Crossroads

We learn that Rickels returned to Germany after his time as a POW and earned his medical degree and did his internships. But he leaped at the chance to return to the United States. The requirement was to spend at least a year at an institute in Iowa. He returned with his pregnant wife, Crista, landing on September 1, 1954. "My dream of a new home was fulfilled."

From his POW experiences, however, Rickels knew that his new home was not a perfect place. At a POW camp in Texas, he found that he was not permitted to share ice water with black laborers; they had to use another ladle – and drink lukewarm water. In 1960, once his family was settling in the Philadelphia area, he found that some real estate salespersons wanted assurances that they were not Jewish.

Rickels soon realized what he wanted to do professionally: "Psychiatry stood at a crossroads. A new type of treatment, namely the potential use of clinically effective medications to treat psychiatric illnesses, had appeared from nowhere. I wanted to be involved in this revolutionary development from its beginning and hoped to become an important player in this new field." With these lofty goals in mind, he applied to be a psychiatric resident at Penn in 1955. It was the beginning of a very successful career, and Rickels has been honored many times for his achievements.

Despite being a pioneer in psychopharmacology, Rickels is not blind to problems in the pharmaceutical industry. He notes stalled drug development in recent years and describes most new drugs as "me, too" drugs with little or no improved efficacy. He also laments the power of marketing departments and the creation of new diagnoses, such as panic disorder and generalized social phobia, which he views primarily as ways to sell more drugs when existing ones are just as effective.

Which takes us back to a comment made about Rickels by a former chair of psychiatry, Peter C. Whybrow, M.D., in *Penn Medicine* (Fall 1988): "Over the years his meticulous studies have given him a revered independence. No drug company can buy Karl Rickels's opinion. Hence, if a company really wants to know the truth and the clinical efficacy of a new psychotropic agent, they seek out Karl Rickels. . . ."

Near the end of his book, Rickels states that the Food and Drug Administration in 2011 approved vilazodone for treatment of adult depression. Its decision was based "on a pivotal study to which my group significantly contributed." The Rickels standard, still in place. ▪

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The old formula was raise the "good" cholesterol and lower the "bad." Thanks to Daniel J. Rader, M.D., we now know it's more complicated than that. For example, he's shown that it's not certain that all HDLs of any type are good. And he's investigating the "efflux" process, which he believes is what makes HDL protective.