

PENN Medicine



WINTER 2009/2010



A PERSPECTIVE ON HEALTH CARE REFORM

Howard Hughes Medical Investigators

Have a License to Think Big

Who's Afraid of CER?

Blue Mothers

Some Strong Words about Health-Care Reform

Fall is in the air, and so is health-care reform. In this issue, you will find three items related to this daunting topic: a Q. and A. with the chief executive officer of Penn's Health System; a column by the dean; and an article on Comparative Effectiveness Research, one of Penn Medicine's strengths.

And in that context, we present Richard "Buz" Cooper, M.D., professor of medicine and a senior fellow at Penn's Leonard Davis Institute of Health Economics.

According to *The Philadelphia Inquirer*, Cooper does not "mince words." An animated audience of Penn faculty members and students can now attest to that fact. Two days after being featured in an *Inquirer* article called "Health-care Heresy?" (November 16, 2009), Cooper was one of the speakers at a campus discussion, "Reforming Health Care: In the Public Interest." The event was organized by Linda Aiken, Ph.D., R.N., professor of nursing and of sociology. Even among the panelists from the School of Nursing and the School of Medicine, Cooper stood out for the boldness of his views.

One of the issues considered was how to expand health care – and primary care in particular. As Cooper put it, it is "a very contentious issue," in part because physician organizations are "so tenacious" about wanting to keep primary care as the realm principally of physicians. "It's mathematically impossible," said Cooper, asserting that there are not enough physicians in primary care now; fewer physicians are attracted to the specialty; and in the not-too-distant future, there will be "horrendous physician shortages" in general.

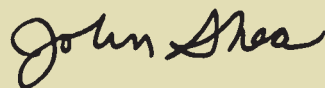
Cooper differentiated between illness care and health (or wellness) care. Physicians, he argued, are trained to do illness care and that on the whole is what

they should do; nurses are trained to do wellness care and prevention, which makes them well suited for primary care. Later in the program, Cooper suggested that if all the surgeons "fell off the face of the earth," society would suffer greatly, because nobody else has their special training and skills. On the other hand, if all the primary-care physicians similarly vanished, there would be other groups equipped to take their place. "In fact," he said, "the more you encourage physicians and deter them from becoming qualified specialists, the more you harm the future health of this country."

Penalties for Hospitals?

Perhaps inevitably, Cooper also returned to one of the main themes of the *Inquirer* article – the push to penalize hospitals in urban areas that spend more (sometimes much more) on their patients, especially their Medicare patients. There are provisions to that effect in the health bill issued by the House of Representatives. "Modern medicine is designed for the people in this room," said Cooper, meaning those who are educated, fairly well off, and speak English. The new provisions would only make matters worse, he argued, and don't take into account co-morbidities and other complications of poorer patients. The Mayo Clinic in Minnesota is often cited for its efficiency and lower costs, Cooper noted, but he added that it is actually "the highest-priced hospital in the upper Midwest."

"Well, now, you take the Mayo Clinic and stick it in North Philadelphia, and let's see how they do," he continued. "Not only that, but they won't even accept Medicaid patients from Nebraska, which is a neighboring state!"



Asked if he would support the health-care reform bills now in Congress, Cooper said it would be a very tough choice but in the end he would. Still, he is concerned about the likelihood of "an enormous bureaucracy" that would weaken the independent authority of professionals, whether doctors or advanced-practice nurses.

Panelist Arthur Caplan, Ph.D., director of Penn's Center for Bioethics, suggested that President Obama's administration to some extent "blew its chance" in the current push, which Caplan calls more about "health-insurance reform" than about health-care reform. And he has not been impressed by some responses from physicians. "The only response I've seen from primary-care doctors right now to current problems is the creation of boutique and concierge medical practices" – an "innovation," he added, "which cuts back on access to primary care and forces you to pay a bounty" to receive it.

On the other hand, another panelist, Mary D. Naylor, Ph.D., R.N., the Marian Ware Professor in Gerontology in the School of Nursing, described herself as more optimistic about health-care reform. She leads a multi-disciplinary program of research designed to improve quality of care, decrease unnecessary hospitalizations, and reduce health-care costs for vulnerable, community-based older people. From her perspective, such nurse-led programs can be very successful – "the evidence is there." A team-based approach, involving on communication and collaboration, can do what a primary-care physician may not be able to. On the whole, Naylor, citing some pilot projects in the works, sees more opportunities for innovation and research, with more reliance on evidence.

And producing and analyzing evidence is certainly part of what academic health systems and professional schools do best. ■

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A LICENSE TO THINK BIG

By Ken Wilan

For a biomedical researcher, being named an investigator of the Howard Hughes Medical Institute brings substantial funding, prestige, and the opportunity to pursue unconventional or high-risk science. Here is a look at the eight Penn faculty members currently in this elite group.

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A PERSPECTIVE ON HEALTH CARE REFORM

By Ralph W. Muller

The nation has gone through many months of intense and sometimes heated discussion about health care reform. Although the outcome is still far from clear, *Penn Medicine* asked Ralph W. Muller, CEO of Penn's Health System, to share his views on health care reform – and what might be in store for the nation and for academic health systems like Penn's.

GENE THERAPY RESTORES PARTIAL SIGHT

By John Shea

In their continuing quest to improve the sight of patients with a rare form of blindness, researchers from Penn Medicine and The Children's Hospital of Philadelphia presented exciting advances with a new set of patients. Each was injected a single time with a copy of a gene they were missing – and all soon reported improved vision in the treated eye.

WHEN WORMS AND ART MEET

Maria Ciocca, a third-year student in Penn's School of Medicine, won third prize in a recent art competition. There was one important requirement: the artists had to use scientific images created during the course of an actual research project. Which is where the worms come in.

COMPARATIVE EFFECTIVENESS RESEARCH: A VALUABLE TOOL FOR HEALTH CARE REFORM?

By Mark Gaige

Although comparative effectiveness research has many boosters – including people in the White House – it also has its detractors, who fear it may lead to putting costs ahead of care. As one prominent Penn practitioner of CER puts it, that view "is exactly wrong." The goal, he says, "is to tailor the right medication to the right people."

BLUE MOTHERS: OUR BROKEN SYSTEM FOR TREATING PERINATAL DEPRESSION

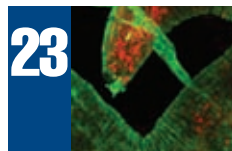
By Erica Rosenberg Tsai, M.D. '09

Practitioners and researchers from several Penn departments are working to provide pregnant women and new mothers with therapy for depression and other mental-health problems. For women in minority communities, getting help is even more of a challenge.

A FEW WORDS ABOUT TRADITION

By Ernest F. Rosato, M.D. '62, G.M.E. '66

Dr. Rosato, professor of surgery, was the featured speaker at this year's White Coat Ceremony for the entering class. He spoke about tradition – "the handing down of information, beliefs, and customs, . . . what bonds us together in a shared remembrance."





Morrisey

\$8 Million for Regenerative Medicine Research

A research team at Penn’s School of Medicine and their colleagues at the University of Washington and the University of Toronto have received \$8 million for stem-cell research. The Penn group is one of nine research hubs awarded \$170 million over the next seven years by the National Heart, Lung, and Blood Institute (NHLBI) to develop the high-potential field of stem- and progenitor-cell tools and therapies. Edward Morrisey, Ph.D., a Penn professor of medicine and of cell and developmental biology, is principal investigator of the grant. He is also scientific director of the Penn Institute for Regenerative Medicine,

The awards create the NHLBI Progenitor Cell Biology Consortium, which will assemble multidisciplinary teams of principal investigators and an administrative coordinating center to focus on progenitor cell biology.

The goals of the consortium are to identify and characterize progenitor cell lines, direct the differentiation of stem and progenitor cells to desired cell fates, and develop new clinical strategies to address the unique challenges presented by the transplantation of these cells. Mor-

risey and colleagues will determine how certain signaling pathways — ordered sequences of biochemical reactions inside cells — affect cardiac and blood-forming cell development and cardiac regeneration and repair. The team will also study whether these pathways may be harnessed for therapeutic applications.

Art and Healing

For the last couple of months, the lofty atrium of the Ruth and Raymond Perelman Center for Advanced Medicine has been the home of nine unusual and

sometimes witty abstract sculptures that have caught the eyes of patients, visitors, and health-care professionals alike. They are part of an art exhibition, “Interplay: Art, Audience, Architecture,” that opened in September and will run through the end of February. “Interplay” is the first exhibition, with two more to follow within the next 18 months. The center is also providing a bi-monthly venue for performing artists. Both forms of art are meant to promote a creative and healing environment. To bring the project to fruition, Penn Medicine worked with the Arts & Business Council of Philadelphia,



a not-for-profit organization dedicated to building partnerships between the workplace and the arts. Shown here is *Composition of 4 Poles*, by Linda Brenner, one of the nine local artists to be represented.

A New Award Seeks to Transform Research

Investigators in Penn's School of Medicine are among the 42 recipients of a new National Institutes of Health award intended to encourage them to challenge the status quo with innovative ideas and to accelerate the pace of discovery. The N.I.H. expects to make competing awards totaling \$30 million through the new N.I.H. Director's Transformative R01 (T-RO1) program. Frank S. Lee, M.D., Ph.D., associate professor of pathology and laboratory medicine, and Stephen Master, M.D., Ph.D., assistant professor of pathology and laboratory medicine, will receive \$1.97 million in total costs over the next five years. Robert B. Wilson, M.D., Ph.D., associate professor of pathology and laboratory medicine, will receive \$1.57 million over the next four years.

Lee and Master will pursue studies on how cells sense oxygen. Work from a number of laboratories, including theirs, has shown that a distinctive chemical modification in cells known as prolyl hydroxylation plays a critical role in regulating a hypoxia-inducible protein known as HIF, which senses low oxygen levels in cells. These studies will have implications for understanding diseases such as heart attacks, stroke, and cancer that are characterized by hypoxia.

Wilson will be working on a novel RNA library of DNA building blocks, which he invented with postdoctoral fellow Yongping Wang, M.D., Ph.D. Their studies have implications for both cell-based and infectious-disease therapeutics.

Dedicating a Center

On November 23, Penn Medicine celebrated the upcoming opening of the Roberts Proton Therapy Center with an event to honor the many donors and staff members who have helped make the \$140 million radiation-therapy facility a reality. When the center opens early in 2010, it will be the largest and most advanced facility of its kind. It will have the capacity to treat – much more precisely than conventional radiation – about 3,000 patients a year.

Among the speakers were members of the Roberts family, which donated \$15 million for the project. As Brian Roberts, CEO of Comcast, put it, “When proton therapy was described, we jumped on it as a once-in-a-lifetime opportunity.”

According to Amy Gutmann, Ph.D., president of the University of Pennsylvania, the new center “represents a quantum leap forward in our capacity to save lives and improve life.”

A Test of Testosterone

Penn's School of Medicine will lead a new \$45 million clinical trial to test whether testosterone therapy can favorably affect certain conditions common to older men. These include decreased ability to walk, loss of muscle mass and strength, decreased vitality, decreased sexual function, impaired cognition, cardiovascular disease, and anemia. Testosterone normally decreases with age, but in some men, low levels of testosterone may contribute to these debilitating conditions.

As the lead institution for the trial, Penn's School of Medicine will serve as the coordinating center. Peter J. Snyder, M.D., professor of medicine in the Division of Endocrinology, Diabetes, and Metabolism at Penn, is the principal investigator and will oversee trial activities. Conducted at

12 sites across the nation, the Testosterone Trial will involve 800 men age 65 and older with low testosterone levels. The National Institute on Aging (NIA) is providing support for this large-scale clinical trial to evaluate the effect of testosterone therapy on older men.

Testosterone products have been marketed for many years to treat a variety of conditions, noted Evan C. Hadley, M.D., director of the NIA's Division of Geriatrics and Clinical Gerontology, which is the primary funder of the trial. “We hope this trial will establish whether testosterone therapy results in clear benefits for older men.”

Ophthalmology's New Chair

Joan M. O'Brien, M.D., professor of ophthalmology at the University of California at San Francisco and director of its Ocular Oncology Division, will assume the chair of Penn's Department of Ophthalmology on January 1, 2010.

Under her direction, the clinical oncology service at UCSF is a leading center for the treatment of ocular malignancies and currently follows one of the largest populations of retinoblastoma patients in the world. Her service is one of only two U.S. centers that specialize in proton-beam therapy for ocular melanoma. O'Brien also directs the Ocular Oncology Laboratory at UCSF, which focuses on developing im-



O'Brien

proved therapies and genetic screening for retinoblastoma.

Throughout her career, O'Brien has been nominated for several teaching awards and has served since 2000 as her department's vice chair for education. As primary investigator on a recent study funded by the Academy of Medical Educators, she developed an on-line study module to quantitatively measure the clinical ophthalmology training of medical students.

Her honors include the Senior Achievement Award of the American Academy of Ophthalmology. She was also the Inaugural Year Recipient of the Physician-Scientist Award, presented by Research to Prevent Blindness. She serves on the editorial board of *Ophthalmology – Journal of the American Academy of Ophthalmology*.

Honors & Awards

Thomas Cappola, M.D., Sc.M., assistant professor of medicine, has received a Presidential Early Career Award for Scientists and Engineers. Cappola was recognized for his research on the causes of and treatment for heart failure, the leading cause of hospitalization among adults in the United States. He will receive up to five years of research support from the National Heart, Lung, and Blood Institute.

Cappola's laboratory has demonstrated that noninvasive genetic tests can be used to diagnose and track transplant patients who may experience rejection of their new heart. This new application of molecular technology may help patients avoid expensive and invasive heart biopsy procedures that are necessary to monitor patients following transplant.

The American College of Psychiatrists has selected **Dwight L. Evans, M.D.**, as its president for 2009-2010. In that role, he will oversee the College's governance and

Pepperpots for P.R., and an Award for Advocacy

PRSA Philadelphia, local chapter of the Public Relations Society of America, recently honored the Penn Medicine Department of Communications with several of its annual Pepperpot awards. The name comes from the pepperpot soup said to have originated during the Revolutionary army's harsh winter at Valley Forge.

Kim Guenther, medical communications officer, received a Pepperpot in Multicultural Communications for "Aging Well: Seniors and Scientists Showcase Experience, Cutting-edge Research from Penn's Institute on Aging." A second Pepperpot went to Rachel Ewing, new media specialist, for "Linking Together: Strengthening Institutional Identity Through Internal Online Communications." The Pepperpot in the Magazine category went to John Shea, editor, for *Penn Medicine* magazine. Holly Auer, senior medical communications officer,

received a "Ladle," the second-highest honor, for her part in placing "Cold Relief," an article on the extraordinary work of the Penn Center for Resuscitation Science, in *Popular Science* (February 2009).

On behalf of the staff of Penn Medicine and its board of trustees, Garry Scheib, COO of the Health System, and Patrick Norton, director of Government Relations and Community Outreach, recently accepted the 2009 Advocacy Action Award. Presented by The Delaware Valley Healthcare Council of The Hospital & Healthsystem Association of Pennsylvania, the award recognizes the employees' leadership and grassroots advocacy efforts on behalf of hospitals, patients, and the Delaware Valley community. Part of the effort involved thousands of Penn Medicine employees who sent on-line letters and petitions to their local state representatives, urging them to oppose the devastating hospital cuts proposed in the Pennsylvania budget.

chair its annual meeting in February 2010. Evans is the Ruth Meltzer Professor and Chairman of the Department of Psychiatry and has appointments in Medicine and in Neuroscience. He also serves as psychiatrist-in-chief for the University of Pennsylvania Health System. A former president of the American Foundation for Suicide Prevention, Evans served as a member of the Institute of Medicine (IOM) Committee on Gulf War and Health in 2008.

George Coukos, M.D., Ph.D., G.M.E. '97, G.M.E. '00, the Celso Ramon Garcia Associate Professor of Reproductive Biology and director of the Penn Ovarian Cancer Research Center, was recently honored by The Sandy Rollman Ovarian Cancer Foundation. He received the foundation's Angela Carlino Excellence in Ovarian Cancer Research/Care Award at its "Fashion Fights Ovarian Cancer"

benefit event. The Coukos laboratory focuses on three areas that revolve around the overarching theme of tumor microenvironment: tumor immune surveillance and tolerance; immune-vascular interactions; and microenvironment editing by tumor cells. Coukos also serves as the associate chief of the division of gynecologic oncology in the Department of Obstetrics and Gynecology.

Kathryn Cunningham Hall, a member of the School of Medicine's Class of 2012, was named one of the 2009 Ten Outstanding Young Americans by the United States Junior Chamber (Jaycees). As a volunteer at Sulayman Junkung General Hospital in Gambia, West Africa, she witnessed many deaths that could have been avoided if the hospital had more than eight to ten hours of electricity a day. In 2006, Hall founded

Power Up Gambia to help provide reliable electricity and water in Gambia through solar energy. She is now working on a second project – to provide solar panels to the hospital's sister clinic. A clinical research assistant at HUP, Hall has pursued a project to confirm the accuracy of a new serum creatinine protocol to aid in kidney flushing.

Jason H. Karlawish, M.D., an associate professor of medicine in the division of geriatric medicine and of medical ethics, is one of 16 scholars across the coun-

try to receive an Investigator Award in Health Policy Research for 2008. Presented by the Robert Wood Johnson Foundation, the awards support research projects that tackle major policy issues, as well as wide-ranging concerns about the nation's health. Investigators receive up to \$335,000. Karlawish serves as associate director of the Penn Memory Center. In his project, "The Making and Unmaking of Alzheimer's Disease," he is exploring how our understanding of the aging brain is changing and raising contentious issues. These include how to define and

treat dementia, the use of neuroimaging, Medicare reimbursement for PET scans, genetic testing, and related matters.

Michael L. Kochman, M.D., the Wilmott Family Professor of Medicine and Professor of Medicine in Surgery in the gastroenterology division, was appointed to the governing board of The American Society for Gastrointestinal Endoscopy (ASGE). Co-director of Penn Medicine's gastrointestinal oncology program, Kochman is a former president of the Delaware Society for Gastrointestinal Endoscopy.

AAMC Honors Two from Penn Medicine

At the annual meeting of the Association of American Medical Colleges in November, two prominent Penn Medicine figures were among the nine individuals and one medical school honored for outstanding contributions to academic medicine.

Arthur H. Rubenstein, M.B.,B.Ch., executive vice president of the University of Pennsylvania for the Health System



Rubenstein

and dean of the School of Medicine, received the Abraham Flexner Award for Distinguished Service to Medical Education. According to the AAMC, Dean

Rubenstein's career epitomizes what was envisioned by Flexner, author of the seminal *Flexner Report* (1910) that led to widespread reforms in medical education in the United States: "a greater emphasis on research as part of the medical education experience; an integrated, institutional focus on learning; and, above all, a joy for the university environment and academic medicine as a profession."

At Penn, Rubenstein has overseen the creation of several interdisciplinary research institutes, including the Institute for Translational Medicine and Therapeutics. Working closely with Ralph Muller, CEO of Penn's Health System, he transformed the flow of funds into a process that is now well-defined, transparent, and equitable for each of the clinical departments.

David A. Asch, M.D., M.B.A., G.M.E. '87 received the Alpha Omega Alpha Robert J. Glaser Distinguished Teacher Award. Asch is the Robert D. Eilers Professor of Medicine and Health Care Management and Economics at the School of Medicine and the Wharton School. According to his students, his focus on inter-professional and inter-school education and collaboration has helped



Asch

them understand the "intricacies of the enigmatic health-care system."

Asch helped establish the joint M.D.-Masters of Science in Health Policy Research program that trains students in health policy research for work in academe, government, industry, and community settings. As executive director of Penn's Leonard Davis Institute of Health Economics, Asch helped develop a summer undergraduate minority research program that pairs students from underrepresented minority groups with Penn faculty to complete research projects.

He is a fellow of the ASGE, the American Gastroenterological Association, and the American College of Physicians.

Virginia M.-Y. Lee, Ph.D., M.B.A., director of Penn's Center for Neurodegenerative Disease Research, was honored with the 2009 Khalid Iqbal Lifetime



Lee

Achievement Award. Presented by the Alzheimer's Association at its 2009 International Conference in Vienna, Austria, the award recognizes Lee's research, which has focused on determining the genesis and roles of various normal and abnormal brain proteins (amyloid, tau, etc.) believed to be instrumental in the cause and progression of numerous brain diseases, including Alzheimer's. A professor of pathology and laboratory medicine, Lee serves as the John H. Ware 3rd Professor in Alzheimer's Research.

Mehret Mandefro, M.D., a Robert Wood Johnson Health and Society Scholar and a senior fellow at Penn's Leonard Davis Institute of Health Economics, was named a 2009-2010 White House Fellow. Raised in Ethiopia, she is a primary-care physician and anthropologist who uses oral histories to teach patients about health care. Mandefro has researched violence prevention and HIV prevention and the use of digital media in translating research. She founded a nonprofit organization, TruthAIDS, to educate patients about HIV prevention, and

IOM Elects Four from Penn

The Institute of Medicine, established by the National Academy of Sciences both to honor achievements in the health sciences and to advise on issues related to health, biomedical sciences, and medicine, has elected four professors from Penn's School of Medicine. The new members bring Penn's total to 72, out of a total active membership of 1,610.

Penn's new members are:

- Thomas Curran, Ph.D., professor of pathology and laboratory medicine and investigator at Penn's Abramson Family Cancer Research Institute
- Frederick S. Kaplan, M.D., the Isaac & Rose Nassau Professor of Orthopaedic Molecular Medicine and chief of the Division of Molecular Orthopaedic Medicine
- Amita Sehgal, Ph.D., professor of neuroscience and investigator with the Howard Hughes Medical Institute

- Garret A. FitzGerald, M.D., the McNeil Professor in Translational Medicine and Therapeutics and chair of the Department of Pharmacology

Curran, who also serves as deputy scientific director at the Children's Hospital of Philadelphia Research Institute, investigates the molecular basis of normal and neoplastic growth of the brain. The goal is to discover new approaches for treating brain tumors in children. A former president of the American Association of Cancer Research, he was on the board of scientific advisors of the National Cancer Institute 2000-2005. In 2005 he was elected to the Royal Society.

Kaplan studies the molecular genetics of FOP and POH, rare bone disorders in which the body forms a second skeleton of heterotopic bone. This collaborative work, conducted with his colleague Eileen Shore, Ph.D., led to the discovery of



Curran



Kaplan

the gene for POH in 2002 and for FOP in 2006. Recognized as the world's leading expert on genetic disorders of heterotopic ossification and skeletal metamorphosis, Kaplan was cited as one of the 15 people "who make America great" by *Newsweek* in 2006.

Sehgal studies the molecular and genetic components of sleep and circadian (or 24-hour) rhythms. Using the fruit fly, she and others have characterized a molecular clock present in flies and in humans. Her laboratory has also developed the fly as a model system for studying sleep, showing that the rest phase in flies is a sleeplike state, helping to answer important questions about the essential need for sleep. She is a recipient of the School of Medicine's Stanley N. Cohen Biomedical Research Award.

FitzGerald is director of the Institute for Translational Medicine and Thera-

peutics. He takes an integrative approach to elucidating the mechanisms of drug action, drawing on work in cells, model organisms, and humans. He has contributed substantially to the development of low-dose aspirin as a therapy, and his team was the first to predict and then mechanistically explain the cardiovascular hazard from NSAIDs. His laboratory was also the first to discover a molecular clock in the cardiovascular system. FitzGerald serves on the peer review advisory committee of the N.I.H..

FitzGerald was also awarded the 2009 J. Allyn Taylor International Prize in Medicine. Supported by the Robarts Research Institute at the University of Western Ontario in London, Ontario, and the C. H. Stiller Memorial Foundation, the \$10,000 prize annually recognizes the world's leading medical researchers.

has produced a documentary film aired on Showtime Networks for World AIDS Day about women in the South Bronx and Ethiopia with HIV. This year, she is among 15 Fellows who will take part in an education program and service projects based in Washington, D.C.

A. Thomas McLellan, Ph.D., an adjunct professor of psychology in psychiatry, was appointed deputy director of the White House Office of National Drug Control Policy, which advises the president and coordinates anti-drug efforts. McLellan has served as executive director of the Treatment Research Institute, a nonprofit center he cofounded to study and compare treatments and to translate scientific findings into clinical practice and public policy. He and his colleagues have developed and evaluated treatments for alcohol and drug dependence as well as evaluation instruments such as the Addiction Severity Index and the Treatment Services Review.

Peter C. Nowell, M.D. '52, the Gaylord P. and Mary Louise Harnwell Emeritus Professor of Pathology and Laboratory Medicine, was named one of the 2010 Franklin Institute Laureates. He received the Institute's Benjamin Franklin Medal in Life Science. Nowell was honored for the discovery (with the late David Hungerford) that alterations to chromosomes can cause cancer, as well as further research that led to the development of a therapy that now cures 95 percent of individuals with chronic myelogenous leukemia.

Peter Quinn, D.M.D., M.D., vice dean for professional services in the School of Medicine, was named the president of the American Society of Temporomandibular Joint Surgeons for the years 2009-2011. The Schoenleber Professor of Oral and Maxillofacial Surgery



Sehgal



FitzGerald

in the School of Dental Medicine, Quinn also serves as a senior vice president of Penn's Health System.

James Shorter, Ph.D., assistant professor of biochemistry and biophysics, has received a New Scholar Award in Aging from the Ellison Medical Foundation. The awards provide support (up to \$100,000 per year for a four-year period) for investigators beginning in the first three years after postdoctoral training, when they are establishing their own labs. Shorter's laboratory investigates how cells achieve the successful protein folding involved in the overwhelming majority of biological functions. In particular, they seek to understand how cells prevent, reverse, or even promote the formation of prions and amyloid fibers. Shorter was an inaugural recipient of the 2007 N.I.H. Director's New Innovator Award.

Louis J. Soslowsky, Ph.D., the Fairhill Professor of Orthopaedic Surgery and the department's vice chair for research, has won the 2010 Ann Doner Vaughan Kappa Delta Award. Presented by the American Academy of Orthopaedic Surgery, it is considered the Nobel Prize in the field of orthopaedic surgery research. Soslowsky, who directs the McKay Orthopaedic Research Laboratory, is also senior author of an article that received the Best Paper Award for this year's meeting of the Association of Bone and Joint Surgeons. The other authors of the paper are **Heather Ansoorge**, a Penn graduate student in bioengineering, and **Pedro K. Beredjikian, M.D., G.M.E. '97**, of the Rothman Institute.

Ben Z. Stanger, M.D., Ph.D., was selected as a 2009 Pew Scholar in the Biomedical Sciences, one of 17 early-career scientists "who display outstanding promise

in research relevant to the advancement of human health." He will receive \$240,000 over four years to support his research. An assistant professor of medicine, he studies how tissues know when to stop growing in order to reach the appropriate size in their own environment. He uses a mouse model to determine how specific genes regulate cell size, division, and death by communicating during development.

Keith L. Wapner, M.D., G.M.E. '85, clinical professor of orthopaedic surgery at Pennsylvania Hospital, is president-elect of the American Orthopaedic Foot & Ankle Society. In this role, he serves on the board of directors of the Society's Outreach & Education Fund. He also was a volunteer in the society's Overseas Outreach Program to Vietnam last year. Wapner is a board examiner for the American Board of Orthopaedic Surgery. ♥



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Questioning Evolution

I am not alone in questioning the veracity of the theory of evolution. All too often the opposition receives little or no attention. George Wald, Harvard professor emeritus of biology and Nobel Prize winner, confessed, “I do not want to believe in God. Therefore I choose to believe in that which I know is scientifically impossible – spontaneous generation arising to evolution.” . . .

Dr. Kenneth Miller, professor of biology of Brown University, takes a different stance about evolution than our Nobel Laureate George Wald (“Two Days in the Year of Evolution,” *Penn Medicine*, Summer 2009). In essence, Dr. Miller must believe in spontaneous generation without which evolution would be impossible. Miller has many fellow believers who really have “faith” in their ideas of evolution. The chromosomes of the chimpanzee as explained being related to human chromosome is indeed a matter of faith, especially “how two pairs got stuck together and fused.” And this had to be a repetitious process forming many similar fused pairs. And ipso facto: Spontaneous generation is indeed true. Louis Pasteur’s conclusion following his monumental work disclaiming this theory, up in smoke? . . .

Why did Darwin indicate that he got “cold all over” when he considered the eye? The rods, cones, macula, rhodopsin (visual purple), the shutter action of the iris controlling light entering the interior of the eye, the lacrimal system providing the required moisture for the cornea. The blink reflex. The required alignment of all the DNA and chromosomes over millions of years to form an eye with its central connections to the posterior occipital cortex. All these structures developing and lining up *by chance*

and aeons so vision would occur. And then there are two eyes functioning consensually needed for depth perception!

My mother had a heart that pumped blood 98 years possessing all necessary systems. Please show me brilliant engineers capable of making a pump with needed systems that would faithfully pump fluid for 98 years. When this occurs, I’ll believe evolution is possible.

Yes, changes within the species, but creating new species all from protein material that just developed by chance with the right temperature, electrolytes, and fluid medium . . . and plenty of time? There is indeed much rational thinking by those doubting the theory of evolution. And might I add that the able presenters, Drs. Miller, Tishkoff, et al., also consider the grand picture that may be missed by knowing more and more of minutiae including chromosomes, DNA, and their observed changes. Step back and try to look at the whole picture.

The photograph of my dear little great granddaughter is submitted. She is the result of evolution? I’ll leave you to ponder that question.

Paul W. Jackson, M.D., G.M.E. ’75
Wallingford, Pa.

Dr. Miller responds:

Dr. Paul W. Jackson writes to “question evolution,” which is certainly his right. However, he pins his skepticism on an unsolved scientific problem, the origin of life, apparently believing that the very existence of such a mystery is fatal to the Darwinian concept of evolution. On this point, he could not be more wrong.

Evolution is a process observed and verified repeatedly in laboratory and field, a dynamic force that leaves testable marks in fossils and genes, and a unifying

scientific theory marked by stunning successes in tying together disparate lines of evidence. Whatever the ultimate origin of life, it is the process of evolution that accounts for life’s great beauty and diversity.

Those who would rise to dispute evolution do themselves no great service when they confuse the classic experiments of Spallanzani and Pasteur on spontaneous generation of flies and microbes with the origin of life. Nor do they strengthen their case when they mistakenly describe evolution as happening “by chance.” Natural selection is not a chance process, and it is the power of cumulative natural selection that produces organs of great complexity, like the eye.

And finally, they would do well to be careful of their sources. Although widely circulated by creationists, the quotation Dr. Jackson attributes to George Wald is not authentic. Dr. Wald’s August 1954 *Scientific American* article on the origin of life, to which this quotation is generally connected, contains no such language. The quotation was constructed by someone, no doubt, who found Dr. Wald’s actual words insufficiently useful as weapons against evolution. I am certain that Dr. Jackson would not have included this misquotation in his letter if he had been aware of that fabrication.

To answer Dr. Jackson directly, I would note Charles Darwin’s own words, that “there is grandeur in this view of life,” and the image of Dr. Jackson’s beautiful great granddaughter is proof of that indeed.

With Best Wishes,

Kenneth R. Miller
Professor of Biology
Royce Family Professor for Teaching
Excellence
Brown University

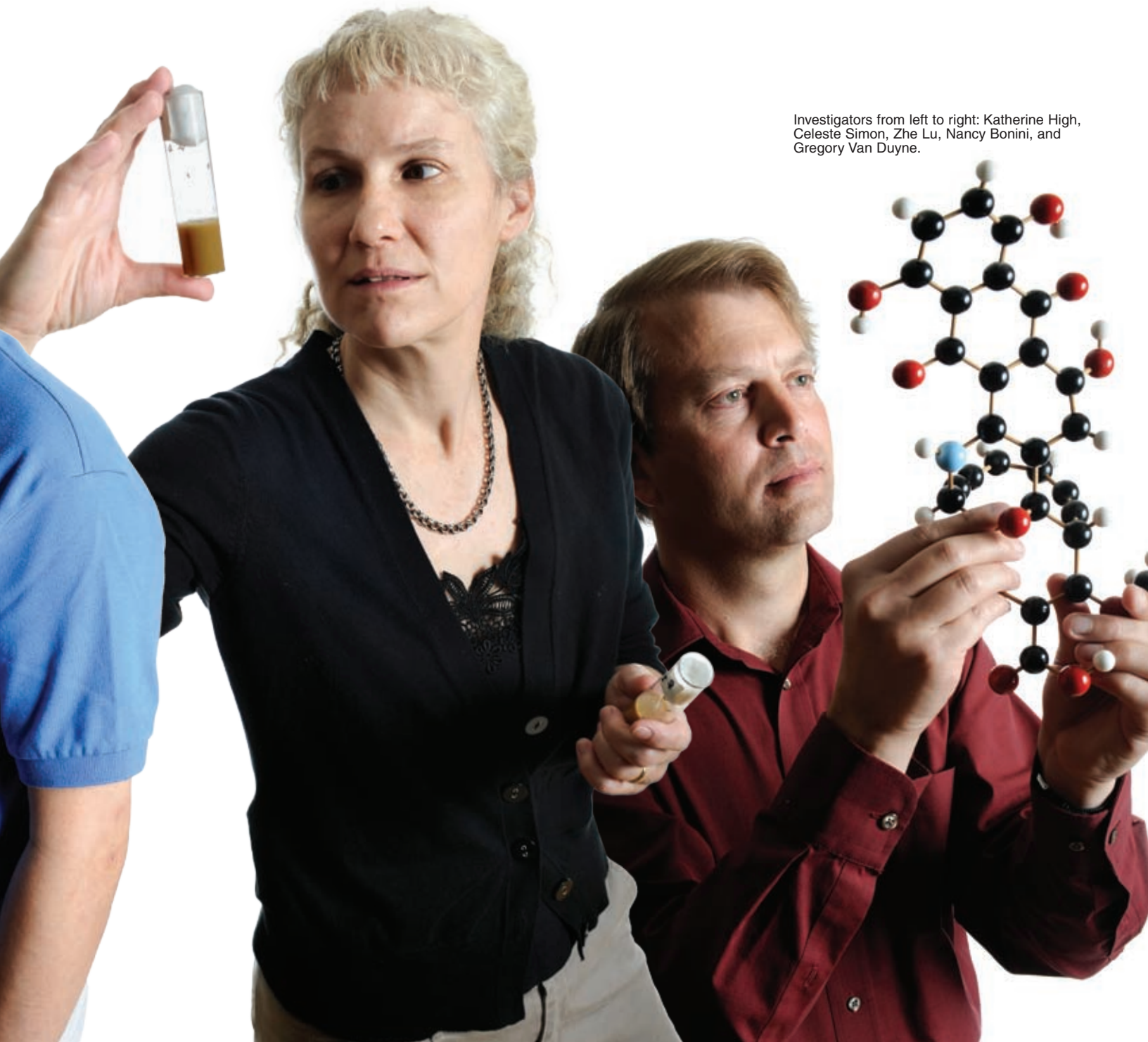
HUMAN A License to Think **BIG**

By Ken Wilan

Photographs by Candace diCarlo



For a biomedical researcher, being named an investigator of the **Howard Hughes Medical Institute** brings substantial funding, prestige, and the opportunity to pursue unconventional or high-risk science.



Investigators from left to right: Katherine High, Celeste Simon, Zhe Lu, Nancy Bonini, and Gregory Van Duyne.

How can we measure a researcher's relative impact on science?

The number of publications and the amount of funding from the National Institutes of Health suggest a relative position in the pecking order of scientists. University affiliation can play an important role in determining the professional life of a scientist as well. Being a member of the National Academy of Sciences, which numbers only about 2,100 scientists and engineers, is among the most prestigious honors. But being selected as an investigator of the Howard Hughes Medical Institute (H.H.M.I.) may have a greater impact. It brings not only prestige but five years' worth of funding.

As of July 2009, there are only about 350 H.H.M.I. investigators in the United States. Perhaps only the Nobel Prize club is more exclusive.

"The N.I.H. is trying to fund all good science," says Glen Gaulton, Ph.D., executive vice dean and chief scientific officer for Penn Medicine. "Howard Hughes is trying to pick *leaders* in the fields."

Celeste Simon and colleague.



Jack Dixon, Ph.D., vice president and chief scientific officer at H.H.M.I., makes a similar point. "We don't fund projects," he explains. "We fund people – and then turn them loose."

Amita Sehgal, Ph.D., the John Herr Musser Professor of Neuroscience at Penn Medicine, has the perspective of the individual researcher. Becoming an H.H.M.I. investigator, she says, "is so prestigious. It means research you are conducting is high profile and cutting edge. Functionally, it gives you a substantial amount of money. One hundred percent of salary, personal supplies, and three or four grants from the N.I.H. would add up to it, but [Hughes] also offers other things. We can ask for big pieces of equipment two or three times a year, and renovation over and above operating budget." Sehgal, who became an H.H.M.I. investigator in 1997, emphasizes that the funding is not restricted. "You can work on anything you want, you can take risks. I'm in the neuroscience department," where she has made significant discoveries about circadian rhythms and sleep. "Tomorrow, if I decide to do immunology, I could." As she put it when she was first appointed, being an H.H.M.I. investigator "allows you to expand, to think big."

Of course, with the appointment come high expectations.

H.H.M.I. offers "unbelievable support, but they don't want one to be productive – they want you to be spectacular," says M. Celeste Simon, Ph.D., professor of cell and developmental biology at Penn Medicine and scientific director of the Abramson Family Cancer Research Institute. Simon has been an H.H.M.I. investigator at Penn since 2000.

THE SOURCE OF THE MONEY

In 1953, Howard Hughes, the industrialist, aviator, and film producer, founded H.H.M.I. for "the promotion of human knowledge within the field

AMITA SEHGAL: UNRAVELING THE MYSTERIES OF



Amita Sehgal, Ph.D., is obsessed with sleep. Since she became an H.H.M.I. investigator in 1997, it is practically all she thinks about. But not in the visceral way a medical student, undergrad, or a post-doc burning the midnight oil might focus on it. For Sehgal, a professor of neuroscience who is associated with the Center for Sleep and Respiratory Neurobiology, it is a scientific quest to understand the molecular basis of the need for sleep.

To do so, she studied the circadian periodicity of the fruit fly *Drosophila melanogaster*. Her laboratory discovered a feedback inhibition loop of two proteins – timeless (TIM) and period (PER) – that regulates a rest/activity cycle. This particular mechanism is conserved in mammals. Sehgal also found regulatory mechanisms that synchronize the fly's internal clock to light and identified the

SLEEP

genetic components that are crucial in the rest/activity cycle.

Receiving the H.H.M.I. appointment has had a significant impact on her research. “If I just had N.I.H grant dollars, I wouldn’t be venturing into new areas,” says Sehgal. “My lab just used to work on clocks. We got into sleep. With H.H.M.I. money, I could go in that direction, and it took off.”

In the time since, Sehgal has developed the fly as a model system for sleep. She has linked the rest phase in flies to a sleeplike state, and she has identified molecular components and cellular loci that regulate sleep as well as how aging affects sleep and circadian rhythms. In addition, she is translating her work with flies to humans, studying the molecular components of endogenous clock functioning and interaction with a person’s behavior and physiology. In one recent study, Sehgal and her team were able to induce jet lag in flies, then reverse it. As she put it, “Over time, we will have a better understanding of how the human clock responds to light and may be able to design drugs to treat jet lag.” Sehgal’s lab continues to explore the regulation of sleep/wake cycles.

Educated in New Delhi and at Cornell University, Sehgal is a member of the American Association for the Advancement of Science. In 1997, she was the first recipient of the Michael S. Brown Junior Faculty Research Award from the School of Medicine. Nine years later, she became the first member of Penn’s medical faculty to receive a second of these Awards of Excellence – the Stanley N. Cohen Biomedical Research Award.

of the basic sciences – principally the field of medical research and medical education – and the effective application thereof for the benefit of mankind.” The institute was granted all 75,000 shares of the Hughes Aircraft Company stock. In 1985, the H.H.M.I. board of trustees approved the sale of Hughes Aircraft to General Motors for an estimated \$5.2 billion (\$2.7 billion in cash and the rest in GM stock). As recently as the late 1990s, in fact, the institute described itself as “the nation’s largest philanthropy.” In 2009, the Howard Hughes Medical Institute, based in Chevy Chase, Md., reported an endowment of \$17.5 billion.

According to its bylaws, every year the institute must spend 3.5 percent of its endowment. Last year, it committed nearly \$700 million for research and distributed more than \$80 million in grant support for science education. Although it opened its Janelia Farm Research Campus in 2006, H.H.M.I. is primarily a virtual institute, supporting its investigators at more than 70 universities, medical centers, and other research institutions throughout the country. At present, there are seven H.H.M.I. investigators at Penn Medicine, including two professors of pediatrics who work at The Children’s Hospital of Philadelphia. Another investigator is a biologist in Penn’s School of Arts and Sciences who also holds an appointment in the Department of Neuroscience. (See “H.H.M.I. Investigators at Penn.”)

At Penn, the H.H.M.I. investigators represent a broad range of fields, including the study of the biogenesis, function, and roles of ribonucleoprotein complexes in human disease (Gideon Dreyfuss, Ph.D.), gene therapy for hemophilia (Katherine A. High, M.D.), and the response of cells to changes in the availability of oxygen (Celeste Simon). According to Craig Thompson, M.D. ’77, professor of medicine at Penn and chairman of the medical advisory board of

H.H.M.I., these investigators represent “very disparate groupings – there is no natural coming together.” Thompson, now director of Penn’s Abramson Cancer Center, is himself a former H.H.M.I. investigator.

H.H.M.I. scientists are engaged primarily in basic biomedical research, although there is growing interest in translational research. Howard Hughes is also looking to fund more patient-oriented work. As Dixon, the institute’s chief scientific officer, notes, “Science research often impinges directly on care, and patients are often part of the experimental paradigm.”

NOMINATING YOURSELF

Although it is exclusive, H.H.M.I. is now also very democratic in a particular way: people can nominate themselves. This is a new development. Until 2007, researchers had to be nominated by their academic institutions, which was permitted to nominate only two or three individuals. In addition, the nominating institution itself had to be chosen by H.H.M.I. Beginning in 2008, any researcher could apply, provided he or she had between four and ten years of experience as a faculty member.

Gaulton welcomes the change. “Every institution has its politics and biases,” he says. “Letting individuals apply directly takes out any biases, and Hughes can sort it out.”

Celeste Simon is another interested party who prefers the new system. “Usually a committee was appointed to represent the entire university,” she explains. “Each department chair nominated a candidate or two.” The nominations went to committee. “Then the dean or provost would decide.” As she puts it, the process could get “pretty political.”

The revised process maintains H.H.M.I.’s focus on selecting investigators who are in early-to-mid career instead of very new researchers or more senior sci-

entists. (Once appointed, however, investigators can continue to be reappointed.) Still, even when they nominate themselves, the candidates who apply tend to be extremely well qualified. “People apply to Hughes only when they know they have a very good chance of success,” says Gaulton. He points out that Penn administrators offer encouragement and assistance to the researchers they believe should apply. The ones ultimately chosen by H.H.M.I. represent not only high standards but also the organization’s desire for geographic diversity among its researchers. In applications, says Dixon, “institutions like Penn and Harvard are almost always overrepresented, but it would be inadvisable to pick people just from Harvard or Penn.”

In 2008, the most recent Penn investigator, Zhe Lu, M.D., Ph.D., was selected with 55 other new investigators – from a field of 1,070 applicants. Lu, a professor in the Department of Physiology who came to Penn in 1996, studies ion channels and their function in genetic diseases such as cystic fibrosis (CF). With Hughes funding, he says, he decides “what is important to pursue. We used to study potassium channels. Now we need to study chloride channels and non-channel-related components in the pathogenesis of CF. We have some unconventional ideas about how to go about this problem.” As he explains, “The N.I.H. supports projects. We write grants on specific projects with specific aims, and you need to address those aims; you can’t change direction.” On the other hand, H.H.M.I. supports laboratories and investigators, so “the Hughes mechanism is perfect to support us.”

THE ENTREPRENEURIAL SCIENTIST

Other H.H.M.I. investigators also note that the Hughes model supports people, not projects. As Gaulton puts it,

the organization gives resources to “very talented individuals for being very talented.” In this way, he says, the model resembles the system in Europe, where government agencies fund people and research areas and tend to give more money to leaders in the field, who then disperse it. A difference, however, is that “the European model is more institutional and senior-driven,” whereas the Hughes model “is very entrepreneurial.”

This entrepreneurial bent is also reflected in the type of person who is successful in becoming an H.H.M.I. investigator. “People talk of a Hughes per-

sonality,” says Morris J. Birnbaum, M.D., Ph.D., a professor of medicine and of cell and developmental biology at Penn Medicine who was an H.H.M.I. investigator for 14 years. “The typical Hughes person is incredibly compulsive, always on top of things. Hughes doesn’t accept peaks and troughs of scientific productivity. A typical Hughes person requires a certain intensity.”

In addition to offering five years’ worth of funding and reducing the need to apply for grants elsewhere, a Hughes appointment offers the scientist a convenient way “to meet other people trying to

GIDEON DREYFUSS: FROM BASIC SCIENCE TO



Gideon Dreyfuss, Ph.D., teases out the critical arrangements between RNA and their bound proteins that determine which messenger RNAs (mRNA) ultimately emerge and how they relay critical information beyond the nucleus. In 1984 Dreyfuss

identified the first definitive group of RNA-binding proteins, and his lab continues to identify new proteins and understand their impact on gene expression.

In 1995, he was prompted to shift some of his focus from basic to translational research when he learned of a discovery across the Atlantic. French researchers had identified a gene mutation that causes spinal muscular atrophy (SMA) disease. Dreyfuss realized that his group had previously discovered the binding protein necessary for the gene, called survival of motor neuron (SMN), to function.

“Everybody knows about muscular dystrophy because of the Jerry Lewis Telethon,” says Dreyfuss. “SMA is almost as common. But not much could be done until the gene and protein were known.”

Dreyfuss and his team then determined how the SMN-protein complex was critical in assembling the building blocks for the cell’s ability to correctly splice the RNAs together. Their findings pointed to splicing errors as a potential



Vivian Cheung

push frontiers,” says Thompson. In this regard, he continues, it is very different, for example, from Keystone Symposia, “where nobody presents anything that hasn’t just been published. At Hughes meetings, because all the investigators are employees, “dialogues are much more open, it’s a different flavor. You’re not worried about patent issues. It’s much more about ‘what could be, how could we do it’ vs. ‘this is what has been done, can you confirm it?’”

H.H.M.I. investigators can choose one Hughes meeting a year to attend; they can also bring along one student. The

meetings in themselves, Sehgal notes, can be helpful in recruiting top people to the lab. In fact, such a meeting helped one of Sehgal’s students land a coveted job. As Sehgal describes it, people in the field may not respond to e-mail requests, but when her student attended the Hughes meeting, “they were happy to sit down with her, they invited her to their labs – and she got an offer.”

At the same time, having the title of H.H.M.I. investigator does not magically lead to better research. “You’re still doing X,” says Vivian G. Cheung, M.D., associate professor of pediatrics at Penn Medicine, whose H.H.M.I. appointment is through The Children’s Hospital of Philadelphia. But, she explains, “you’re hoping to do X more deeply and elegantly with the additional resources.”

In addition to dollars, the Howard Hughes resources include access to equipment and administrative services via the H.H.M.I. office in Penn’s Clinical Research Building. The office serves faculty with Penn appointments as well as those at other institutions in the mid-Atlantic region. These include Children’s Hospital, Princeton University, Rutgers University, and the University of Medicine and Dentistry of New Jersey. The office is located at Penn because of its central location and because Penn has the most investigators in the region. The help provided by the H.H.M.I. office is not insignificant. According to Laurie Cassel, who heads the office, it includes assistance with personnel matters; budgets; supplies and equipment; and facilities management. Also important is ensuring that all the laboratories comply with the host institution’s environmental health and safety programs.

For an institution, Hughes investigators represent bragging rights. Gaulton points out that there are other investigators at Penn who have more funding than Hughes people, but H.H.M.I.

POTENTIAL THERAPIES

cause of a form of the disease. In 2008, Dreyfuss showed that mice deficient in SMN have decreased amounts of ribonucleoproteins in different cells, which bolstered the connection between SMA proteins and the progressive muscle wasting caused by decreased motor neurons in the spinal cord.

The lab’s next step was to develop screening assays for drug therapies that would increase the SMA protein. But to make use of the assays, they needed an appropriate “library.” They eventually found one at Merck & Co. Here, H.H.M.I.’s focus on innovation in medical research and its broad experience in managing collaborations came into play.

“H.H.M.I. and the University had the skill and foresight to facilitate a program like this,” explains Dreyfuss. “How do we protect all sides – for H.H.M.I. and Penn to have the investigative freedom to pursue anything, not work for profit, and publish results?” At the same time, he continues, Merck needed assurance that its “crown jewels” would not be revealed.

“And there was my commitment to develop compounds for SMA patients. This was not your typical material-transfer agreement.”

According to Dreyfuss, academe and pharmaceutical companies are working together now on a different scale, and the relationship offered Merck the opportunity to refine a template for academic collaboration. Although it took a year, the arrangement was finalized. Merck performed the screen, and both institutions are now studying the top hits.

Dreyfuss earned his B.Sc. degree in chemistry and physics at the University of Jerusalem and his Ph.D. degree in biological chemistry at Harvard University. A member of both the American Academy of Arts and Sciences and the European Academy of Sciences, he received the Established Investigator Award of the American Heart Association. He was the first recipient of the Stanley N. Cohen Biomedical Research Award, one of the Awards of Excellence presented to the most distinguished members of Penn Medicine’s faculty.

H.H.M.I. INVESTIGATORS AT PENN

University of Pennsylvania School of Medicine:

Gideon Dreyfuss, Ph.D. The Isaac Norris Professor of Biochemistry and Biophysics

Dreyfuss explores the biogenesis and function of ribonucleoprotein complexes and their roles in human disease.

H.H.M.I.: 1990-present

Zhe Lu, M.D., Ph.D. Professor of physiology

Lu investigates the fundamental mechanisms by which ion channels accomplish a variety of biological tasks, including mediating communications between neurons, controlling the rate of the cardiac pacemaker, coupling blood glucose levels to insulin secretion, and maintaining a balance of fluids and electrolytes. His research has shed light on the pathology of cystic fibrosis, and his laboratory is working on ways to inhibit the toxins that cause certain bacterial infections.

H.H.M.I.: 2008-present

Amita Sehgal, Ph.D. The John Herr Musser Professor of Neuroscience

Sehgal investigates circadian rhythms and sleep.

H.H.M.I.: 1997-present

M. Celeste Simon, Ph.D. Professor of cell and developmental biology

Simon investigates hypoxia, angiogenesis, and tumor progression. As she told *H.H.M.I. News*, "Oxygen is absolutely essential for life, so the biological mechanisms underlying response to low oxygen are central to the cell." Because tumors have been able to survive in low-oxygen environments, research in this area could lead to ways to block their protective response and prevent them

from developing the blood vessels they need to grow.

H.H.M.I.: 2000-present

Gregory D. Van Duyne, Ph.D. The Jacob Gershon-Cohen Professor of Medical Science, Department of Bio- chemistry and Biophysics

Van Duyne is interested in the molecular mechanisms that cells use to maintain and process the information contained in their chromosomes. With Frederic D. Bushman, Ph.D., professor of microbiology at Penn, Van Duyne was a senior author of a study that determined the structure of an important smallpox virus enzyme and showed how it binds to DNA. A recipient of the Michael S. Brown Junior Faculty Research Award, Van Duyne was described at the time by his department chair as "one of the premier young structural biologists in this country who knows how to approach and answer fundamental questions in biology and medicine."

H.H.M.I.: 2000-present

Children's Hospital of Philadelphia:

Vivian G. Cheung, M.D. The William Wikoff Smith Endowed Chair in Pediatric Genomic Research Associate professor of pediatrics and of genetics

Considered a pioneer in building and using DNA microarrays, Cheung seeks to identify the genetic determinants of human traits and to develop tools that make such studies easier and more accessible. Her team uses combinations of molecular and computational methods to study basic genetic mechanisms and those related to human diseases. Genetics, she has argued, should be "a foundation of predictive and preventive medicine." She is a member of the American Society for Clinical Investigation.

H.H.M.I.: 2008-present

Katherine A. High, M.D. Director, Center for Cellular and Molecular Therapeutics The William H. Bennett Professor of Pediatrics

High investigates the molecular basis of disorders of blood coagulation and novel approaches to treatment. Having had success in treating hemophilia in mice and dogs, she is now focused on adapting the therapy for humans. Former president of the American Society of Gene Therapy, she recently led a team at the Center for Cellular and Molecular Therapeutics that developed a vector (a genetically engineered virus) that delivered a gene to human patients with a form of congenital blindness; the clinical trials were successful in partially restoring the patients' sight.

H.H.M.I.: 2003-present

University of Pennsylvania:

Nancy M. Bonini, Ph.D. The Lucille B. Williams Professor of Biology

Bonini studies mechanisms of human degenerative diseases, including Huntington's, Parkinson's, and Alzheimer's diseases. Her research team has created models for human neurodegeneration in the fruit fly. Using *Drosophila* to define the genes involved in the mechanisms and progression of polyglutamine repeat diseases, they are trying to identify suppressor mutations that can prevent or delay brain degeneration. In earlier studies also using fruit flies, Bonini studied *eyes absent*, a gene that controls eye development. Her honors include the Basil O'Connor Award from the March of Dimes and the John Merck Scholars Award in the Biology of Developmental Disabilities in Children.

H.H.M.I.: 2000-present



Katherine High displays a model of a vector for delivering genes.

offers steady “hard” money as well as a convenient way to compare research institutions. (For example, there are 16 investigators on the H.H.M.I. site listed with Harvard Medical School or Harvard

University.) In contrast, awards from the American Heart Association or the MacArthur Foundation, to cite two leading sources of funding, are not renewable. “Having a lot of Hughes investigators is considered prestigious for the individual and institution,” says Gaulton. “We would love to have more and more.”

ALUMNI INVESTIGATORS

For individual scientists, however, there can be a down side.

“Most scientists are searching for a yardstick to measure success,” says Birnbaum. “You do it by looking to your peer group, at your institution, or in your field. The moment one gets into H.H.M.I., it is perfectly acceptable to judge your own success or failures by other H.H.M.I. researchers across the country.” The problem, he continues, is that, for some researchers, “this can be intimidating and depressing. It’s all compounded by the knowledge that this is not only an initial comparison, but you will be judged by a panel” after five years of support.

Fifteen percent of investigators will not be asked back; after that point, they cannot reapply.

“Losing the title, I would imagine, would be really upsetting,” says Sehgal. “Some of the people who lost it are really good scientists and did well after it. Almost everybody I know who’s left Howard Hughes has done terrific work, though at the time I would imagine it is quite devastating.”

From all appearances, H.H.M.I. remains proud of what it calls “alumni investigators” and maintains a section devoted to them on its Web site. At present, there are 11 alumni investigators listed who were associated with Penn during their time with Hughes, and most of them are still on campus.

One of those alumni investigators is Birnbaum. Appointed an H.H.M.I. investigator in 1994, he passed two reviews. On his third five-year review, however, he was not reappointed.

“With N.I.H. grants, you can resubmit. H.H.M.I. is the equivalent of three or four grants all coming up for review at the same time,” says Birnbaum, who calls the system “very intimidating.”

“I thought having all this money, not dependent on N.I.H. funding, would relieve this pressure. It was exactly the opposite,” he says. “I found the Hughes was much more pressure than being a typical Harvard or Penn faculty member trying to get tenure and a lab funded. The criteria are much more stringent than how an institution judges for tenure or the N.I.H. for grants.”

Still, while the appointment lasts, Birnbaum emphasizes that the Howard Hughes Medical Institute offers a researcher the freedom to do high-risk science. In his own case, he explains that funding from H.H.M.I. was crucial for a discovery made in his lab: understanding how cell or organ growth in the fruit fly is regulated via signaling pathways. “I never would have been able to move as fast with N.I.H. or other grants.

“There is no doubt it is worth it.” ▀



Gideon Dreyfuss: an expert on spinal muscular atrophy.

A PERSPECTIVE ON HEALTH CARE REFORM



AFTER MANY MONTHS OF INTENSE PUBLIC INTEREST and sometimes heated discussion, the U.S. House of Representatives and Senate finally presented bills on health care reform. Although the outcome is still uncertain, *Penn Medicine* asked Ralph W. Muller, CEO of the University of Pennsylvania Health System, for his views on several aspects of health care reform – and what might be in store for the nation and for an academic health system like Penn’s. Muller, who became CEO in 2003, has a distinguished record in health care administration and policy. Among his many appointments, he has served on the Medicare Payment Advisory Commission and the board of directors of The National Committee for Quality Assurance. He has been chairman of the Association of American Medical Colleges, the Council of Teaching Hospitals and Health Systems, and the University Healthsystem Consortium.

Q. Has the time really arrived for significant health care reform? Are all the forces in fact aligned as we have been led to believe? Or will reform be only incremental and postpone the crisis for another two or three years?

A: Health care reform is likely to pass; there is a tremendous political imperative for the President and the Democratic Congress to pass legislation. Although what we will have may be imperfect, it is an important first step toward a focus on higher quality and increased access to health care for the American people.

On the other hand, change will not be immediate. The Kaiser Family Foundation recently found that about half of the public believes that if reform passes, help for the uninsured and insurance coverage reforms would arrive by the end of the next year. In reality, the proposed legislation is stretched over several years. For

example, in the recent Senate bill, the first individual mandate penalties don’t kick in until 2014.

Q. What will be the consequences of no health care reform or a weak version of it for the nation? For academic medical centers (AMCs)? Will the status quo grow worse?

A. Penn and other academic medical centers have performed well in the current system, even with the large amount of charitable care provided to uninsured patients; however, society as a whole cannot afford to have people without health care insurance. Therefore, simply postponing the pain of reform could lead to a more abrupt shock to Penn and AMCs in the future.

Penn Medicine has invested in several areas directly related to health care reform – for example, through quality and

safety initiatives – and we believe we will be best positioned to lead within this environment where there is significant attention to high-performing health systems.

Q. What role can academic medical centers play in supporting health care reform? Do you believe that AMCs have a responsibility to support reform? What role do you see for Penn Medicine as a particular institution?

A. Academic medical centers deliver the most advanced care to a broad range of patients, including the poorest. We have an absolute responsibility to support reform that sustains a health care system that reaches as many patients as possible and gives those patients access to high-quality, affordable health care.

Specific actions that Penn Medicine can take include focusing on developing efforts that support our system-wide

“Blueprint for Quality” initiatives and ensuring that we are providing efficient, high-quality care. Our successful initiatives include cutting our preventable re-admission rates and reducing healthcare-acquired infections.

Penn Medicine should also participate actively in novel arrangements between physicians and hospitals, such as Accountable Care Organizations (ACOs). And because Penn hospitals are integrated with most of our physicians, we are better able to look at ideas like “bundled payments” and ACOs.

Q. Are there current models in other nations that embody a reformed health care system?

A. Every nation has a health care system that reflects both its moral and economic priorities. For example, the United Kingdom operates the National Health Service (NHS), which directly finances health care and operates the hospitals. The NHS provides health care to all U.K. permanent residents – for free at the point of need and paid for from general taxation.

In Germany, compulsory insurance applies to those below a set income level and is provided through private non-profit “sickness funds” at common rates.

The United States is much larger geographically than the United Kingdom, Germany, and their European peers. What about Canada? Size, however, is not the only variable – the U.S. also has a far more diverse population than Canada. Our expanse, volume, and heterogeneity, as well as the individualistic culture we thrive upon – all these factors have shaped the health care system we have today and the one we will change with reform. It follows that the health care reform debate in the United States is taking place in the context of our American values.

Q. Can you review with us why you think Medicare reform based on geographi-

cal disparities (as outlined by the *Dartmouth Atlas of Health Care*) is a faulty premise?

A. The Obama Administration has placed a great deal of faith in the *Dartmouth Atlas*’s suggestion that if spending in high- and medium- cost areas were reduced to the levels seen in the lowest-spending areas, Medicare spending would then be reduced by up to 30 percent. These savings would be achieved by eliminating so-called inefficiencies in the system. However, while this approach may feel like logical policy, much of the variation in health care spending is based

Academic medical centers deliver the most advanced care to a broad range of patients, including the poorest. We have an absolute responsibility to support reform that sustains a health care system that reaches as many patients as possible and gives those patients access to high-quality, affordable health care.

on differences in physician care patterns that are difficult to change and in policy choices made over the years, such as recognition of the differences in the cost of living across the country and support of high-performing teaching hospitals.

If we look more closely at the basis of the “30 percent savings” theory, we see that the core argument is based on Medicare expenditures, and it attributes most of the variation to “regional factors” in clinical practice. The matter is much more complicated than that. Medicare

payments are not representative of the total resources available to hospitals and MDs. Medicare payments are not the total spending on Medicare patients; supplemental plans are also important.

The academic literature has shown numerous factors that affect costs: the patient’s health status; the presence of advanced medicine in teaching hospitals; and the price and cost of living. Dartmouth appears to adjust for these factors differently than other sources. Health status drives utilization, and there is disagreement that the Dartmouth methodology captures differences in health status. There are variations in utilization, but they are driven less by geography and more by local physician practice patterns, which can be studied and adjusted.

Our experience over many years has taught us that poverty is a key factor, because it affects the need for care and the ability to follow up on treatment. Race and previous lack of insurance also appear to be correlated with higher expenditures, which indicates the impact of life-long trends in access to care.

AMCs bring all these elements together: teaching, serving the poorest, serving the sickest, and operating in high-cost urban areas. These are essential parts of what we do.

Q. What are the highest priorities for the nation? For AMCs? Some of the publicized goals are: reducing costs; providing better, higher-quality care; providing wider or universal health-insurance coverage; increasing the primary-care work force; increasing the physician work force in general; and maintaining disproportionate share payments (DSH).

A. As I’ve mentioned, the argument of the *Dartmouth Atlas*, which is endorsed by Peter Orszag, director of the Office of Management and Budget (OMB), is that Medicare will be able to pay less because of greater efficiency and value. But

wringing efficiencies out of the system is not as easy as waving a wand. It requires changes to physician practice and acceptance of evidence-based medicine.

It is important not to lose sight of two key priorities that must be considered while pursuing cost efficiencies: educating future physicians and caring for the poorest. This is why Penn and other AMCs have advocated strongly for preserving teaching and DSH payments.

Both the nation and academic medical centers will benefit from wider health insurance coverage, higher-quality health care, an increase in primary-care physicians, and maintaining disproportionate share payments. More coverage provides access to care for patients while also supporting AMCs that provide uncompensated care. Penn Medicine has long provided such care. At the same time, DSH payments help urban medical centers to take care of our indigent patients.

Q. What is comparative effectiveness research in the context of the nation and of Penn Medicine?

A. On the national level, comparative effectiveness research (CER) is being funded by The American Recovery and Reinvestment Act (ARRA), which approved \$700 million for comparative effectiveness research at the National Institutes of Health and an additional \$400 million at the Department of Health and Human Services. The Institute of Medicine issued a report establishing priority areas. The stated focus will be comparing clinical efficacy; there will not be an official link between cost-effectiveness and coverage.

At Penn Medicine, we have established the Center for Evidence-Based Practice, which summarizes scientific evidence for UPHS decision-making about high-impact drugs, devices, and processes of care. The center is also charged with building evidence-based collaborative enterprises with outside organizations. This

group analyzes not only technologies but also processes such as effective practices for reducing blood-stream infections.

Q. How deep must insurance reform be for sustainable reform of our nation's health care system? What would that look like?

A. Reform should focus largely on the need for people to be covered; both the House and Senate bills do so. The House bill will see an additional 36 million Americans gain health insurance, while the Senate proposal plan will provide

Our expanse, volume, and heterogeneity, as well as the individualistic culture we thrive upon – all these factors have shaped the health care system we have today and the one we will change with reform. It follows that the health care reform debate in the United States is taking place in the context of our American values.

access to coverage for an additional 31 million Americans beyond those currently insured. The legislation provides subsidies to insure people and mandates to enforce participation.

As we pursue reform of health care delivery through insurance reforms, we must not repeat the mistake made in the 1990s, when providers entered the insurance business. Yes, we must experiment with reform, but I firmly believe that insurers should insure and health care providers should provide health care. Forwarding

the risk to providers is not practicable, and it does not benefit the patient.

Reform of the payment system requires the insured set of patients to be large enough to absorb the cost of the varying health needs of all individuals. What will not work is a return to straight or fixed capitation, as we had in the 1990s, which simply shifts the insurance risks to providers in small geographic areas.

Q. How is Penn Medicine uniquely positioned to take advantage of health reform when it comes?

A. We will be in a very strong position because of several factors. We have the research expertise to come up with novel ideas around the high-value delivery of health care. In our “Blueprint for Quality” and related initiatives, we have a multi-year focus on quality improvement that is becoming embedded into our operation.

In addition, we have tight integration with our physicians, including CPUP (the Clinical Practices of the University of Pennsylvania) and CCA (Clinical Care Associates, our primary-care network), which allows us to take advantage of evidence-based medical practice.

We also have a leadership team that is familiar with health policy and very engaged in following how reform will be implemented.

Q. What about the medical side of health care reform? What is the role of the patient in all this? What can be done from the patient side to help keep down costs and improve the quality of care?

A. The short answer is healthy living and wellness.

Patients can help enormously if they invest time in their preventative care and adhere to therapeutic plans. Their personal commitment to taking care of themselves has tremendous potential for improving quality of life and avoiding unnecessary costs in the health care system. ♥



Gene Therapy Restores Partial Sight

Corey's Team: Corey Haas, center, has the support of, from left to right, Dr. Katherine High, Ethan Haas, Nancy Haas, and Dr. Jean Bennett.

The star of the October press conference was the smallest and youngest person in the room. While two of the researchers summarized what they called “spectacular” advances in treating a rare form of blindness, Corey Haas, a nine-year-old blond boy with glasses, sat quietly with his parents. He was barely as tall as the auditorium stage. But later in the event, when he was called to come up on the stage and sit with the scientists who led the clinical study, the 4th-grader had no trouble in leaving his seat and confidently finding his way.

That was not always the case. In fact, a little more than a year ago, Corey Haas had great difficulty finishing an indoor mobility course that simulates a street route. The course tests how much a person can see and how much light their eyes detect. In the classroom, Corey needed special equipment, large

print projected on an electronic screen, to read. He was understandably hesitant about riding his bicycle or trying to play softball. He was, in fact, legally blind. Corey has a rare retinal disease called Leber’s congenital amaurosis (LCA), caused by a mutated gene that keeps people’s bodies from producing a necessary protein. As a result, the photoreceptor cells in the eye eventually die. At present, there is no treatment for LCA, and Corey would likely become totally blind.

The press conference had been arranged so that the researchers could present the findings of their gene-therapy study, which was to be released online ahead of publication by *The Lancet* (October 24, 2009). Conducted by researchers from Penn Medicine and The Children’s Hospital of Philadelphia, the study extended a smaller, preliminary study published in *The New England Jour-*

nal of Medicine in May 2008. There, the researchers reported on the success they had with twins in their early twenties, but, based on animal studies, they were confident the gene therapy would have a greater impact with younger patients. Corey Haas is the youngest of the newer group, which includes four other children and seven adults.

Engineering a Vector, Administering a Gene

At the press conference, Katherine A. High, M.D., the co-first author of the *Lancet* study, was the first to speak. The William H. Bennett Professor of Pediatrics at the School of Medicine, she is director of the Center for Cellular and Molecular Therapeutics, the facility at Children’s Hospital that sponsored the clinical trial and manufactured the vector that carried the gene, RPE65, that pa-

tients with LCA are missing. High noted that rare diseases are often not commercial enough to attract drug firms. She also talked about developing the vector, a genetically engineered adeno-associated virus, looking to “optimize it” for safety and efficacy.

High was followed by Jean Bennett, M.D., Ph.D., the F. M. Kirby Professor of Ophthalmology at Penn, who is the senior author of the study. The other co-first author, Albert M. Maguire, M.D., associate professor of ophthalmology, was in surgery at the time – as Bennett put it, “in the trenches, actually preventing blindness!” It was Maguire who gave each of the 12 patients a copy of the missing gene, via a single injection. Given the experimental nature of the study, each patient was injected only in the eye with weaker vision. And within two weeks, all 12 subjects reported improved vision in the treated eye.

The result, as High put it, “is an exciting one for the entire field of gene therapy.” High, who is also an investigator of the Howard Hughes Medical Institute, noted that the current findings “may expedite development of gene therapy for more common retinal diseases, such as age-related macular degeneration.”

Measuring Success

A reporter asked how the success of the trial was measured. Bennett cited both subjective and objective tests. Facing the same mobility course that formerly baffled Corey Haas, the younger subjects were able to navigate it quickly and confidently. The researchers also used pupillometry to measure the receptivity to light: ten participants in the trial improved by two orders of magnitude. Corey’s father, Ethan Haas, told the reporters that he and his wife, Nancy, noticed a change almost at once. Corey’s

pupils, which had been very dilated, were significantly smaller.

It was Bennett who asked Corey to come on stage. “This is absolutely incredible to me, and very emotional,” she said. She asked Corey to describe some of the changes he’s experienced. Riding a bike? Before, it was inside his house in Upstate New York – or not at all. And now: “I just take off” and ride around the neighborhood. At school now, “I can recognize people by their faces, not just their voices.” While reporters went on to ask their questions, Corey answered patiently. Another change: he sees colors much better.

His father said having to watch as Corey’s condition got worse “was tearing me up.” But now Corey plays by himself, goes to visit friends – and sometimes has to be called inside even when it’s dark. And although his vision is nowhere near 20/20 at this point, Corey is no longer legally blind.

As the researchers emphasized, however, LCA and related retinal diseases are progressive. Treating the photoreceptor cells, said Bennett, amounts to “a race against time.” When asked if he’d like his other eye treated, Corey immediately answered “yes!” But the researchers must be prudent.

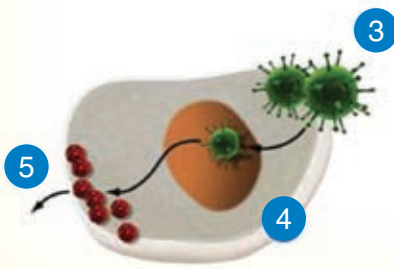
Still, as Bennett put it, they have arrived at “an incredible launching pad” that she believes will help them to study other genetically based diseases and to develop gene augmentation strategies to treat or prevent them.

In the meantime, as Bennett reported, the oldest patient in the LCA trial, a 44-year-old mother, had been unable to walk down the street to meet her children at school. Since the treatment, she has even watched her daughter hit a home run. And we hear that, up in Hadley, N.Y., Corey Haas has been smacking some of his father’s underhand pitches. ▀

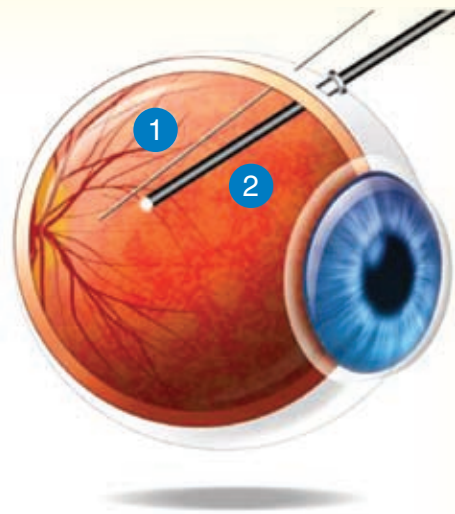
– John Shea

How it Works

Using DNA, scientists create a functioning gene to replace the faulty one in the retina. Then they place the new gene inside a little “coat” made up of viral proteins (known as a vector). The type of virus researchers use does not have the ability to reproduce or cause disease.

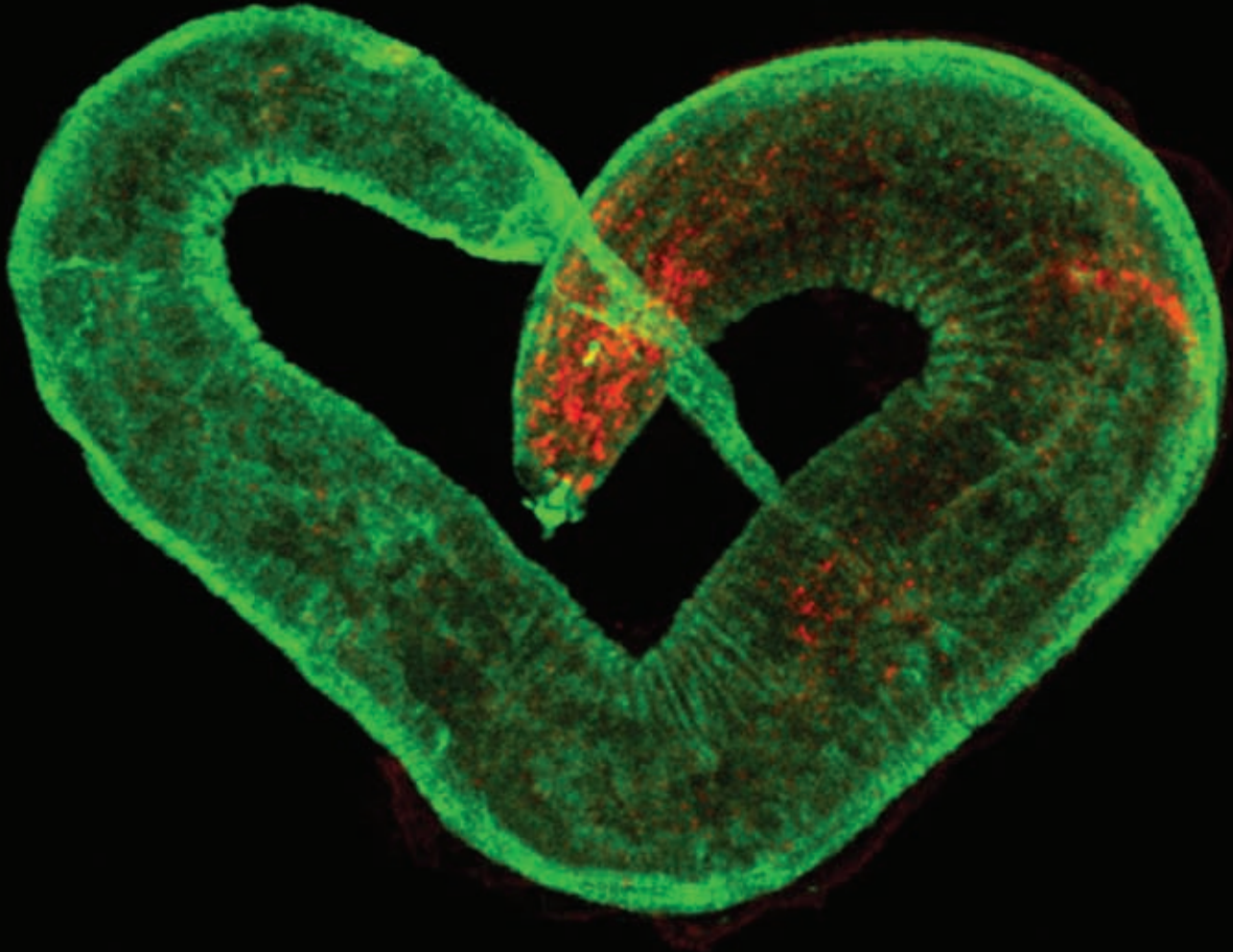


Scientists add in the new gene by injecting it directly into the eye (above) through a thin needle (1) connected to a syringe, with the help of a light probe (2). The new gene (3) enters the cell nucleus (4), where it makes the healthy enzymes (5) required to see.



Children's Hospital of Philadelphia

When Worms and Art Meet



EARLIER THIS YEAR, Princeton University held its third Art of Science competition, whose purpose is to explore the interplay between science and art. Of the more than 200 submissions from undergraduates, faculty members, research staff members, graduate students, and alumni, 48 works were selected to go on line (<http://www.princeton.edu/artofscience/2009/>), and the top three prize-winners were announced at a gallery opening. This year's theme was "found art," but the artist-scientists

were asked to use scientific images created during the course of an actual research project. And it was an alumna, Maria Ciocca, now a third-year student in Penn's School of Medicine, who won third prize. Her submission: *Worm Love*.

Ciocca explains how the image came about: "I am a graduate student in a lab that studies the process of asymmetric cell division in the development of model organisms, such as the nematode *Caenorhabditis elegans*, pictured here. In the process of using immunofluores-

cence microscopy to study the one- and two-cell stage embryo of this organism, occasionally the slides will contain fully developed worms that were not properly removed in the fixation process. . . . When I came across this image, it was too good to pass up." As she notes, however, the worm's natural shape does not include the sharp kinks shown in her image, which here form the base of the heart. Nor does the worm typically assume a shape resembling a heart. But that's where the artistry comes in. ♥

COMPARAT EFFECTIVE RESEARCH:

By Mark Gaige



IVE NESS

THE ADVOCATES OF CER POINT OUT THAT IT'S
BASED ON EVIDENCE, WILL LEAD TO BETTER
HEALTH CARE, AND IS SORELY NEEDED IN A TIME OF
BURGEONING COSTS. OPPONENTS
CLAIM IT WILL LEAD TO RATIONING
AND PUT COST AHEAD OF CARE.

A VALUABLE TOOL FOR HEALTH-CARE REFORM?

Once again, it seems, Mom was right. When she told us to shop around and not rush to buy the first thing we see, a sizable number of faculty members at Penn Medicine – Kevin Volpp, Katrina Armstrong, Brian Strom, Sean Hennessy, Kendal Williams, and Craig Umscheid among them – must have been paying close attention.

Each of them engages in comparative effectiveness research, or CER, which evaluates how well medications and therapeutic devices and procedures work for given medical conditions. In effect, it is comparison shopping for health care. CER relies on objective analyses of treatments and costs to settle on the best treatment or medication. Sometimes CER confirms that established practices work best; other times it doesn't.

But even within CER, their approaches and areas of interest are by no means identical. Brian L. Strom, M.D., M.P.H., the George S. Pepper Professor of Public Health and Preventive Medicine who serves as chair of the Department of Biostatistics and Epidemiology, and Sean Hennessy, Pharm.D., Ph.D., associate professor of epidemiology, have extensive experience in the more traditional forms of CER. For example, Hennessy did a study comparing two anti-depressants to see whether, when used in an intensive-care unit, one led to more frequent

aspiration and pneumonia. As Strom explains, a patient might vomit, inhale the vomit, and develop pneumonia from it. Hennessy's study made clear that the drugs were *not* different.

Although the terminology was different, Strom says, "We've been doing these kinds of studies since the 1980s, when we looked at relative frequency of gastrointestinal bleeding from different nonsteroidal anti-inflammatory drugs. We had studies of anaphylaxis and neutropenia, when the number of the white blood cells goes down, and how they differed among the different NSAIDs."

According to Strom, there are three fundamental steps in CER. The first is to synthesize the data that is already out there – which is basically evidence-based medicine. The second step is to generate new data, which Strom says is mostly what Penn Medicine historically has done. The third step is working to have the data implemented in practice.

Kevin Volpp, M.D. '88, Ph.D., has been conducting a different kind of research. What pushed him into CER was observing the patients in his own clinical practice. Year after year they would try to quit smoking or lose weight, largely without success, even when they were at high risk of serious health problems or premature death.

“These were people using conventional medical approaches that did not work. Something new had to be tried.”

That something is now called “pay for performance for patients.”

“What my colleagues and I are doing is CER in action. In our case we’re examining whether paying someone to quit smoking or lose weight works better than traditional medical approaches. We are examining, in essence, whether shifting some of the money used to treat diseases in the future can be used to motivate people to engage in healthier behaviors *now*.”

In an opinion piece in *The New England Journal of Medicine*, Volpp and co-author Anup Das write: “If CER’s full potential for improving the population’s health is to be realized, . . . comparisons must go beyond those between medication A and medication B or device A and device B: we must also assess medications or devices in comparison with behavioral interventions, either alone or in conjunction with other approaches” (July 23, 2009).

Volpp, who has a Ph.D. degree in health economics from Penn’s Wharton School in addition to a Penn medical degree, is director of the Center for Health Incentives in Penn’s Leonard Davis Institute of Health Economics. “Given my economic training, it was natural for me to think about financial incentives while seeing patients struggling to change their behavior, since much of economics has to do with understanding how people respond to prices and incentives.”

The Leonard Davis Institute is one of very few research centers that test whether insights from behavioral economics can help patients make healthy choices. “In many cases” says Volpp, “patient behavior is the proximate cause of disease. For example, obesity is a major risk factor for hypertension, diabetes, lower back pain, and other conditions. Patients who are able to lose weight may be able to reduce



Photo by Tommy Leonard

Kevin Volpp

or eliminate their use of medications for these conditions. Therefore it makes sense to compare medication-based approaches to the treatment of diabetes with behavioral approaches to weight reduction.”

Volpp and his colleagues tested the different approaches in a study that received international attention earlier this year (*NEJM*, February 12, 2009). They found that smokers who were offered financial incentives of \$750 were almost three times as likely to stop smoking for 18 months – 9.4 percent versus 3.6 percent. In addition to providing a new tool to help people contend with a fiendishly obstinate addiction, the findings, Volpp says, underscore the importance of innovative thinking in seeking out better alternatives to help patients. The findings “are showing that behavioral interventions can often serve as a useful complement or lower-risk substitute for medical treatments in many clinical contexts. CER enables us to examine a range of credible treatments to see what works best.”

The Right Time, The Right Climate

Why CER and why now? When asked if the economic and political environment is more conducive today than ever before,

Brian Strom has a quick answer: “Vastly.”

To a great extent, the convergence of the nation’s continuing economic downturn and President Obama’s push for health-care reform has sparked calls for greater attention to what works best in medicine. According to the Congressional Research Service, by 2009, national health-care spending will total \$2.5 trillion, or 17 percent of gross domestic product. The Congressional Budget Office projects that it may increase to 25 percent of GDP in a few years. Such daunting numbers have led policy makers, clinicians, and academics to offer a raft of new proposals to contain costs and improve quality.

At the same time, earlier approaches are being dusted off, reconfigured, or given new prominence. CER is one such technique and it has been gaining renewed attention. In decades past, the thinking behind it could be detected in pharmacoepidemiology, which applies epidemiologic approaches to studying the use, effectiveness, and safety of drugs in large numbers of people. Clinical epidemiology has a broader scope. As Penn’s Center for Clinical Epidemiology and Biostatistics, which was created in 1993, explains on its Web site, “Clinical epidemiologists investigate the frequency, outcome, prognosis, etiology, treatment, prevention, diagnosis, costs, and policy implications of disease.” More recently, CER has absorbed part of that mandate under a new name, generating much debate, some concern, and often high expectations for delivering better care at lower prices.

CER seeks to identify best-in-class remedies. In some situations, choosing the best option for a medical problem is straightforward. In other cases, the challenge becomes picking the one that will do the most good and least harm. Unfortunately, for many clinical problems there have been few, if any, high-quality studies that compare plausible treatments. Usually

the studies compare patients receiving individual treatments to untreated patients or patients receiving placebos – not to each other. CER, which uses head-to-head comparisons whenever possible, aims to put such testing and therapeutics into clearer perspective. Its supporters also point to its potential to help explain unequal health outcomes among subsets of the population – for example, the varying survival rates for African-Americans and whites for certain types of cancer.

Comparisons for any given medical condition under CER can take a number of forms besides the more familiar drug-to-drug study, including:

- one kind of surgery to another
- a particular drug to surgery
- drugs and surgery together to surgery alone or drugs alone, and
- one technology to another (Which heart valve is better?)

As Volpp's examples show, CER also examines non-surgical and non-pharmaceutical options. For example, for patients suffering from emphysema, a recent trial compared exercise to lung-volume-reduction surgery. And "watchful waiting" is not discounted.

CER has received a boost in the form of substantial new federal funding. Following a 2007 Congressional Budget Office report that highlighted its promise for delivering high-quality care in an efficient manner, Congress appropriated \$1.1 billion to support CER as part of the economic stimulus bill – far more than the \$50 million the government spent in the 2009 fiscal year. Some of it will be spent via the National Institutes of Health, some via the Agency for Healthcare Research and Quality, and much of it is still to be distributed. Some of the new funding will be used for comprehensive reviews of published scientific studies, some will be used for new epidemiological studies, and some will be used for new clinical trials that directly compare

different treatments. The legislation also created the Federal Coordinating Council for Comparative Effectiveness Research to coordinate federally funded CER research and advise the president and Congress on how to spend the money.

The CBO report noted that "the relative scarcity of rigorous data about comparative effectiveness . . . means that decisions about what treatments to use often depend on anecdotal evidence, conjecture, and . . . judgment of the individual physicians involved." Focusing on the cost-effectiveness potential of CER, the report concludes that "generating additional information about comparative effectiveness . . . would seem likely to reduce health-care spending over time."

As Strom points out, Peter Orszag, the White House budget director "really, really believes in CER. . . . The political climate is completely different."

But not unanimously in favor of CER, by any means.

Facing Opposition

While few people question the potential clinical benefits of comparing treatment options for medical conditions, introducing cost-effectiveness into the picture, as suggested by both the CBO report and a report from the House Appropriations Com-

mittee, has ignited sometimes strong opposition among some clinicians and policymakers. They fear that government health programs (including Medicare) and private insurers may use CER results to deny coverage for treatments deemed less cost-effective. Representative Charles Boustany, Republican of Louisiana, a heart surgeon, says that "I'm just deeply concerned about cost alone being a factor in making clinical decisions." He also raised the possibility that "federal bureaucrats will misuse this research to ration care, to deny life-saving treatments to seniors and disabled people" – based on clinical judgments made not by their doctors but by others.

Among elected officials, concerns about cost-effectiveness research are not confined to Republicans. For example, Representative Allyson Y. Schwartz, Democrat of Pennsylvania, urged that the federal government guard "against the use of this research to deny access to care solely based on cost."

Some observers wonder if insurers will demand study after study before reimbursing a medical product or procedure. This tactic, they warn, could delay treatments, harm patients, raise prices, or hamper innovation.

Part of the opposition to comparative effectiveness research is highly organized. *The Wall Street Journal* reported that "the drug and medical-device industries are mobilizing," portraying CER as "the first step to government rationing" (February 10, 2009). According to the *Journal*, a coalition called the Partnership to Improve Patient Care includes the lobbying arms of those industries as well as some patient-advocacy groups. The article notes that, in 1995, when the Agency for Healthcare Research and Quality suggested that there were too many unnecessary back surgeries, doctors and industry groups attacked its conclusions. As a result, Congress slashed the agency's budget and stripped part of its authority.



Brian Strom

Photo by Sabrina Louise Pierce



Katrina Armstrong

As Brian Strom puts it, “There are a lot of industry people who are petrified about [CER] and are looking for any reason to try to undercut it. . . . Companies would rather compete on their marketing ability than on the utility of their product. The key distinction here is, right now, they compete based on marketing, and what CER would do is force them to compete based on the utility of the product.”

While the debate continues, CER has been building a track record. For years, state Medicaid programs, the Veterans Health Administration, and a number of private health plans have been using the approach. For example, Siri Childs, Pharm.D., the pharmacy administrator for Washington State, told *The Washington Post* that comparative effectiveness research has made it possible for Washington State to trim its Medicaid spending on drugs by \$40 million a year (March 17, 2009). A recent article in *NEJM* reports on how Washington State’s evidence-based health policy has affected decisions about which forms of health technology will be covered by the state. Although several challenges remain, the authors say that a conservative estimate of first-year savings would be \$21 million (October 29, 2009). And four years before the Food and Drug Administration pulled the anti-inflammatory agent Vioxx from the market, CER

researchers at Kaiser Permanente health plan removed Vioxx from its formulary; they had concluded that the medication was no better than lower-priced alternatives and that in some cases it seemed to increase the risk of stomach bleeding or heart complications.

A Growing Presence at Penn

For Katrina Armstrong, M.D., M.S.C.E., professor of medicine and associate

director of Penn’s Abramson Cancer Center, CER represents a dynamic tool for addressing a number of her research interests, including cancer disparities. Armstrong recently received a grant under the national economic stimulus package – one of the highly competitive GO (Grand Opportunity) grants – to create Penn’s Center for Comparative Effectiveness in Genomic Medicine. It will be housed at Abramson.

A FORERUNNER WHO’S STILL RUNNING

Brian L. Strom, M.D., M.P.H., may not have been there when comparative effectiveness research began – and, in fact, the name of the discipline has changed over the years – but he certainly established himself as one of its leading proponents. He is the editor of an influential text, *Pharmacoepidemiology*, now in its fourth edition. The George S. Pepper Professor of Public Health and Preventive Medicine, Strom serves as chair of Penn’s Department of Biostatistics and Epidemiology and director of Center for Clinical Epidemiology and Biostatistics.

Earlier this year, Congress allocated \$1.1 billion to CER. Strom has long pleaded the case for more CER and especially for post-marketing studies to compare drugs’ safety and effectiveness. This fall, Strom spoke to John Shea of *Penn Medicine* on the issue. Here are his some of his forthright thoughts on CER.

Defining the Topic

Most CER deals with drugs. Most drugs are studied before they are released on the market in the U.S., based just on studies done comparing active drugs to placebos. In fact, the FDA requires that at the present. And there is a good scientific reason why that’s the case. In

order to find out whether it *does* work, you need to compare it to something that doesn’t have an active ingredient in it.

But there are at least three very, very key pieces of information that are not known at the time that a drug is released on the market. First, does it work in the real world as opposed to the ideal world? Because pre-marketing studies are conducted in the context of clinical trials, with people who don’t have other diseases, don’t have other drugs, don’t have other conditions – a very homogeneous population. What happens out in the real world, when you don’t have somebody whipping you to take the drug?

The other question is, how does the drug work compared to available alternatives? It’s in the interest of the sponsors to show the drug works compared to *nothing*; indeed, they are required to. However, they usually don’t want to test it against an older alternative because the newer product might not be any better, especially given that the newer one is probably much more expensive.

You come to a doctor with your high blood pressure or with your high cholesterol – which blood pressure med do you use? Often, it’s whichever one gave the doc the best dinner. And so medical de-

Genomics is the study of all the genes in an organism, including people, as well as the interactions of those genes with each other and the environment. “CER will become increasingly crucial in the field of genomic medicine,” says Armstrong. “Advances in genomics can improve health care by targeting interventions to individuals who will derive the greatest benefit and experience the lowest risk of adverse events. More effective tar-

geting, which CER will help us achieve, is important because it is one of the few approaches that can both improve outcomes and reduce costs – the unquestioned sweet spot of health care reform.”

Genomic medicine, she notes, has a long way to go before it arrives at that sweet spot. In particular, much more information is needed about whether clinical genetic tests can accurately predict if a person will develop a certain disease,

whether the tests improve clinical outcomes, and whether using them makes sense given costs that are frequently high and possible objections on ethical grounds. Armstrong and her colleagues will examine these questions and others through statistical and modeling analysis of genomic tests that are currently in use or will soon be. Among the first studies planned, the Center will examine tests for predicting a person’s propensity to

decisions are made based on personal relationships with marketers instead of being based on what makes the most medical sense. CER is intended to address that issue – to determine which of the alternative treatment regimens works best. And it doesn’t have to be comparing two drugs. It can be drug versus surgery or drug versus watchful waiting.

The third piece of information that CER provides is that not every drug works in every patient. If you can identify which patients are most likely to get a good response from the drug, you can restrict the drug to the people likely to benefit. The flip side is that we could steer the drug away from people likely to suffer a safety problem. That’s the kind of information companies don’t want you to get because they don’t want to sell the drug only to the people it works on. They want to be able to sell the drug to everyone, and then they try to carve out as big a market as possible.

Rationing and CER

The accusation that CER leads to rationing of care is exactly wrong. It leads to *optimal* care. If the answer is that the more expensive drug is the better one, then the answer is to use more of the expensive

one. The idea is to lead to *better* care, not cheaper care. To the degree it leads to “don’t use the drug in this person because it’s not going to work in that person,” that is a kind of rationing that’s good. Right now, the rationing is based on who has the money to pay for it and which detail men bought the latest lunch, as opposed to rationing based on therapeutic choice.

Right now, we *have* rationing of care. It’s rationing based on cost. Which of the different statins is the managed-care organization going to push? It’s going to be whichever they get the best price on from the manufacturer. What CER does is provide *clinical* data to make these choices. So if there’s going to be rationing, it can be based on data, which again might end up with *higher* costs in some cases.

Marketing and Conflict of Interest

Many drug companies would rather compete on their marketing ability than on the utility of their product, depending on the product. The key distinction here is, right now they compete based on marketing; what CER would do is force them to compete based on the utility of the product. There are some companies that are saying, “We’re fine. We’re happy to compete based on the quality of our

product.” There are other companies that are scared to do that. But again, it’s not just Pharma companies. It’s technology. You know, the issues in many ways can be even worse when it comes to hip replacement or valve replacement. Right now, there is an enormous amount of – essentially – physician bribery. In the case of orthopaedic surgeons and cardiologists, the issues of conflict of interest can be enormous. Right now, those decisions – for example, which hip gets put in – are being made by the surgeon, who could sometimes be on the payroll of a company. And the hospital and then ultimately the insurance system pays the bills for whatever product is ordered, which can be extremely expensive.

The primary effect of CER will be to be able to do say which hip should go into whom and when, and which is better and which is worse, based on data and not based on financial ties. Technology companies are much more scared than Pharma companies because Pharma companies have data. The device companies have almost no data – and the number of docs making the decisions in terms of orthopods and cardiologists is small. They’d much rather just try to bribe the doc – because there is no countervailing force.

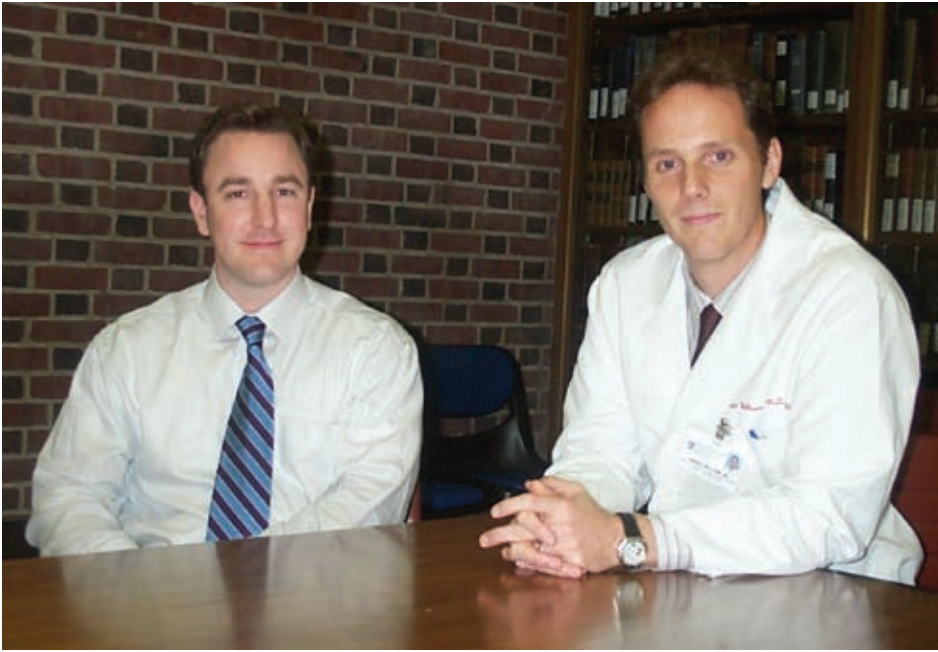


Photo by Sally Saepaga

Craig Umscheid, left, and Kendal Williams

nicotine addiction. (Earlier studies have shown that “slow metabolizers” and normal metabolizers respond differently to transdermal nicotine.) Another study will investigate screening for breast-cancer risk and prevention. As Armstrong notes, “Currently, only 15-33 percent of women who undergo biopsy for an abnormal mammogram actually are found to have cancer,” so improved accuracy would better inform clinical decisions.

For the past three years, the Center for Evidence-Based Practice (CEP) has been providing a continuing case study in how CER operates. Under the direction of Kendal Williams, M.D. '95, M.P.H., and Craig A. Umscheid, M.D., M.S.C.E., both assistant professors in the Department of Medicine, the center has been conducting comparative assessments of drugs, medical devices, and methods of delivering care, then sharing its findings throughout Penn's Health System.

The center, says Umscheid, “helps create and promote a culture of evidence-based practice, which is the very heart of comparative effectiveness research. Large research and teaching hospitals are

beginning to see the value these types of entities can generate, both in terms of more effective care and better deployment of financial resources. Patients get the benefit of what works best, and hospitals can channel savings produced by CER into high-need areas – which is increasingly important as hospital costs rise in the face of decreasing reimbursements and insurance coverage.”

More than 90 CER reports have been completed since P. J. Brennan, M.D., the Health System's chief medical officer, created the center in 2006. Most assessments are carried out at the request of medical, nursing, or administrative leaders.

To prepare a guideline, members of the center's staff first meet with those making the request to gain a better understanding of the issue. (In addition to its co-directors, both of whom are trained in epidemiology, the center includes two analysts, a librarian, a health economist, and specialists in primary care and infectious disease.) They then convene a task force of clinical and research experts from within UPHS to examine the issue from a variety of perspectives. Next,

representatives of the center review the medical literature, extract the relevant data, and prepare summaries for the task force to evaluate. The group grades the evidence for overall quality. Individuals from outside of the task force, including industry liaisons and other UPHS clinicians, may be invited to discuss the reports and their assigned grades. Finally, the task force develops a clinical practice guideline based on its evaluations and discussions. CER reports with grades have been completed on several topics, ranging from the particular – the use of chlorhexidine for preventing surgical site infections – to the general – best practices for discharging inpatients.

According to Williams, there are challenges to operating a CER center. First, centers “need to balance academic rigor with operational efficiency to complete reports in a timely way so that they can affect decisions. Working with leaders to prioritize projects and using existing reviews when available can help achieve this.”

Second, it can be difficult to consider costs effectively when published cost analyses are not available. When such information is critical to a decision, however, the analyses can be carried out in house with cost data specific to the hospital. Third, health-care providers who are not formally trained in evaluating evidence can sometimes be less open to processes informed by CER. The center can usually overcome such reluctance, says Williams, by involving stakeholders from the start “and making decisions in a fair and consultative manner.”

A recent CEP evaluation involved the question of whether to use saline or heparin to flush central venous catheters. The use of heparin to flush such catheters has been an accepted practice for decades. Heparin is thought to prevent the catheter from developing clots that could decrease or prevent flow through the catheter and also become a potential

site for infection. But the anticoagulant also presents a risk of heparin-induced thrombosis, whose consequences can be life-threatening. Working with the chair of the review committee, CEP analyst Matthew D. Mitchell, Ph.D., found 22 papers that met the criteria to be included in the analysis. After examining the evidence, the review committee concluded that flushing with heparin is no more effective than flushing with saline alone. In light of these findings, published in the *Journal of Advanced Nursing* (September 2009), the nursing policy for maintaining central venous catheters was changed to flushing catheters *only* with saline. Following this change, catheter-associated bloodstream infection rates have continued to decline, there have been no increases in catheter or vein occlusion, and the workload of nurses has been reduced without compromising patient safety.

Another practitioner of CER at Penn is Sean Hennessy, Pharm.D., Ph.D., associate professor of epidemiology and of pharmacology. He is the Health System's principal investigator within the DEcIDE (Developing Evidence to Inform Decisions about Effectiveness) Network, a national consortium of research-based health organizations that conducts practical studies about the outcomes, comparative clinical effectiveness, safety, and appropriateness of health care items and services. "I like the basic science underpinnings of research," he says, "but I decided many years ago that I prefer studying populations rather than engaging in basic science research. I enjoy examining the big picture and am gratified when I find results that can be of benefit to large groups of patients." Hennessy recently won a highly competitive "challenge" grant from the N.I.H. as part of the stimulus package. The goal is to create a data infrastructure from several major sources and to use the linked data to perform research on drug utilization and



Sean Hennessy

CER. In particular, Hennessy is seeking to gather data on "typically underrepresented populations."

"The very nature of what I do is integral to DEcIDE's mission, which includes systematically reviewing and synthesizing evidence on treatment effectiveness and identifying knowledge gaps. Addressing gaps is important because interventions that are effective under a highly specific set of circumstances often fail to replicate across a wide variety of settings, conditions, patients."

Brian Strom has published and lectured worldwide on clinical epidemiology – a prototype for CER – for 30 years and edits the major textbook in the field. As principal investigator of a Center for Research and Education on Therapeutics (CERT), Strom is an active participant in the CER debate and disagrees with its critics on many counts. Because CER helps identify which patients are most likely to get a good response from a particular drug, "you can restrict the drug just to the people likely to benefit. We could also steer the drugs away from people likely to suffer a safety problem." The overall goal of Penn CERT is to decrease inappropriate

use of antibiotics, which reduces resistance to antibiotic drugs.

Strom disputes an inevitable link between CER and rationing of care, which, he asserts, "is exactly wrong." Instead, he says, "It leads to *optimal* care. If the answer is that the more expensive drug is the better one, then the answer is use more of the expensive one. To the degree it leads to 'don't use the drug in this person because it's not going to work in the person,' that is a kind of rationing that's good."

Some opponents claim that CER will result in "cookbook medicine," since only certain approved interventions would be reimbursed. Again, Strom disagrees. "Certainly people are afraid of the cookbook, one-size-fits-all kind of medicine. In fact, the goal of CER is exactly the opposite, which is to tailor the right medication to the right people."

Strom does not shy away from the cost-effectiveness debate. In the context of health-care reform, he says that "If we can identify the right drug for the right patient, health care becomes much more efficient. You're not giving drugs that don't work to people. You're able to give cheaper drugs to people if they work as well as more expensive drugs; and in general you decrease the cost of care."

Still, Strom does not view CER as a panacea. "CER should, over time, decrease costs and lead to improved care. But it's not going to shrink costs short-term. . . . We don't even have enough investigators to do the studies now. And those studies will take a number of years to do."

In the end, as Strom puts it, "CER is research to find out what works and what does not." Comparative effectiveness research provides data to make choices – informed choices – among many alternatives, an approach that seems increasingly attractive in today's environment when health care varies in quality and costs steadily increase.

Mom would likely agree. ♥

Deborah Kim., M.D., is testing the safety and efficacy of Transcranial Magnetic Stimulation for pregnant women. Taking the role of a patient here is Susan McKenzie, a crisis counselor in the Department of Psychiatry.



BLUE MOTHERS:

OUR BROKEN SYSTEM FOR TREATING PERINATAL DEPRESSION

Many pregnant women with depression and other mental-health problems fail to receive therapy that could help them through this particularly intense period and beyond. For women in minority communities, getting help is even more of a challenge.

By Erica Rosenberg Tsai, M.D. '09
Photographs by Addison Geary



Women with depression during pregnancy are lucky if they get linked up with Marian Moseley, M.S.S., M.L.S.P. The mental-health system is so complicated that Moseley, a social worker in HUP's Helen O. Dickens Center for Women's Health, must refer to an extensive chart she has created to figure out where these women can go to get help. The behavioral health clinics, scattered throughout Philadelphia like birdseed, differ depending on each patient's insurance and neighborhood. These days, obstetricians, psychiatrists, pediatricians, and family doctors are often literally miles from each other. And no single group seems to know what the others are doing to confront the problem they all see – depression during and after pregnancy.

"If I had more time, I'd try to talk with the different mental-health docs to see how they're working on getting people into care better," Moseley says. But no one, it seems, has enough time. So the specialties remain isolated.

Because none of the psychiatrists practices in the Dickens clinic, Moseley's next task after locating the proper clinic is helping the women get there. Nearly 95 percent of the pregnant women in her inner-city clinic are on Medicaid, so barriers stack up: transportation, child care, inflexible jobs, clinic hours that do not accommodate working schedules, and lack of support.

"When women get shuttled from ob-gyn offices to psychiatry offices, it reinforces the idea that they're going somewhere that's out of

the ordinary," says Ian Bennett, M.D., Ph.D., assistant professor in Penn's Department of Family Medicine and Community Health. "It's a metaphor – but it's real." Bennett knows from his own research that people are much more likely to go to a psychiatrist if the office is right down the hall they're familiar with. The stigma of mental illness is so powerful that many people, especially those from poor minority communities, distrust the mental-health system and the antidepressant medications they are prescribed; often they view depression not as an illness but as a weakness or a symptom of the stress caused by poverty or other factors they alone must face.

"Many people don't perceive their emotions as something medicine can help with," Bennett says. "They may view the best treatments for depression as getting a job, a boyfriend who is supportive, child-care resources. The medical perspective is that all that would be easier to achieve if their depression is under control."

The prevalence of Major Depressive Disorder is 8 percent in non-pregnant women (and about the same in pregnant women), with a slightly increased risk postpartum. That's why health-care workers can scarcely avoid tackling this challenge head on. But solutions don't come easily. Although pregnant women have more contacts with health-care professionals during the perinatal period, it is complicated by multiple transitions in care – from primary care to obstetrics to pediatrics – in just a few short months.

For women

Tanisha Johnson and her child, Manayzian Harris, visit with James Guevara, M.D., associate professor of pediatrics.



A POLITICAL AND SOCIAL ISSUE AS WELL

The mental health of pregnant women and new mothers, long the concern of the women themselves and their health-care professionals, has entered the sphere of politics in recent years. The Melanie Blocker-Stokes Postpartum Depression Research and Care Act (H.R. 20) has been passed by the U.S. House of Representatives and is slated to come before the Senate at some point. The act is named for a young mother who suffered from postpartum psychosis, the most severe form of postpartum depression, and who killed herself three months after giving birth to a daughter. H.R. 20 would require the National Institute of Mental Health to conduct and support basic and clinical research, epidemiological studies, diagnostic techniques, and informational and educational programs to increase understanding of the causes of the condition and to search for a cure.

Bobby L. Rush, a Democratic Representative of Illinois, first introduced the legislation in 2001. The original act now includes additions from the Mothers Act, proposed by Senator Robert Menendez (Dem. from New Jersey).

without private insurance, prenatal Medicaid coverage ends after pregnancy, at precisely the time when new moms are busier and more financially stretched than ever. Low-income women have it especially tough, but they are the least likely to make it through the clinic door.

“We need to make sure that we don’t just throw up our hands,” says Bennett. “Instead, we need to switch our frame of reference from one that is based on years of experience with people who show up” to a system that is really public-health oriented and is focusing on, or including, the people who don’t show up.”

Physicians at Penn aren’t overlooking this population. Doctors who see these

One of the organizations strongly in favor of the act is Postpartum Support International. According to its Web site: “Postpartum depression is a serious and disturbing condition that affects approximately 1 in 7 new mothers, resulting in about 800,000 new cases each year. Of the new postpartum cases expected to be diagnosed this year, fewer than 15 percent of mothers will receive treatment.”

The act also has critics among women’s groups and medical professionals. A recent article in *Time* argues that much of the controversy centers on screening. Although the current act does not specifically mandate funding for testing for postpartum depressions, critics expect greater use of screening if the act passes. One disagreement: “Does PPD screening identify cases of real depression or simply contribute to the potentially dangerous medicalization of motherhood?” (*Time*, July 10, 2009). In addition, other critics of the Blocker-Stokes Act claim that screening results in many false positives.

— John Shea

depressed women – specialists in obstetrics, pediatrics, primary care, and family medicine – are all looking for solutions.

James Coyne, Ph.D., a professor of psychiatry at Penn, is the primary investigator of an R01 grant from the National Institute of Mental Health (NIMH) to study the experience of women who are depressed during pregnancy and postpartum. Along with Bennett and the rest of his multidisciplinary team, Coyne will observe the attitudes and beliefs of both women and their physicians concerning the nature of depression and depression treatment, what helps and what hinders, and what is effective and what isn’t.

Coyne has a broad outlook, in part because he spends time in Europe as a



Bernadette Wheeler, M.D., advocates for built-in mental-health

consultant to the European Commission, analyzing models of depression care in 17 regions of Europe. Back in the United States, he works with what he’s got. “If the health-care system changes here – maybe we’ll have universal health care soon like parts of Europe – then I’ll have some great solutions, because I know what works and doesn’t work in that setting,” he says. In the meantime, however, he believes he has “some creative things we can do.”

According to Coyne, two big problems make providing and receiving care for depression difficult in the United States. First is the fragmented system. In Europe, people retain their “medical home” – a primary-care doctor who follows them throughout their lives – instead of being shuttled from one specialist to the next. In addition, the stigma of mental illness and of seeking help is enormous here, whereas in Europe, Coyne says, “people aren’t so expected to take care of themselves.” His NIMH study will help identify such barriers in this country at the system level and the individual level.

In the current fragmented system, Coyne wonders “to what extent can we train the women to look after themselves, to over-



services for poorer patients.

come stigma and barriers and be effective consumers of health care – or attach navigators to them to guide them through? To me, those are the two possible solutions to an otherwise impossible task.”

Because pregnancy is a time of increased contact with the health system, Coyne suggests that midwives and home health aides could serve as more effective navigators. He also proposes using technology such as the Internet or telephones to aid care. Health-care professionals could flag electronic records with reminders to contact women about depression after pregnancy or to urge them to restart medications they had stopped during pregnancy.

Bernadette C. Wheeler, M.D., a clinical assistant professor of obstetrics and gynecology, has a double perspective on mental-health care for pregnant women. She divides her time between two very different obstetrics clinics in Penn Medicine’s system. She is medical director of the Helen O. Dickens clinic, where 95 percent of patients are on Medicaid, and she also works at Penn Medicine at Radnor, which predominantly treats a middle-class, mostly Caucasian population. “It plays out differently,” says Wheeler.

Marian Moseley, M.S.S., M.L.S.P., helps patients navigate the complicated mental-health system.

“The way I see it, the people who get the best psychiatric care are basically rich.” The conclusion seems to be that no system currently has enough funding to provide ideal mental-health care unless patients pay for it themselves. And most people are unable to do so even while employed full time.

At Radnor, where most patients pay out of pocket for medical care, a psychologist has an office located inside the obstetrics clinic. Stacked next to Wheeler’s business cards are the psychologist’s business cards – a sign of implicit approval.

“Let’s get some funding so we can have built-in mental-health services in a poor population,” says Wheeler. She points out that the Dickens clinic has two social workers who help with many issues related to mental health – but they’re not psychiatrists or psychologists.

As Wheeler puts it, “The more educated someone is, the more likely they will say mental-health problems are part of being a human being.” But for many in the lower economic strata, “it’s a weakness,” she says. “They don’t think of depression as a disease. Instead, you’re not praying enough, you’re not doing enough. The stigma is very strong in the African American community.”

Wheeler went into obstetrics to be a health advocate for women during important junctures in their lives. “In

women’s health, there are many critical times,” Wheeler says. “Pregnancy is a great opportunity for change. It seems a mental-health piece during pregnancy is very important because it’s going to not only help mom but also her fetus.” Indeed, studies show that children of mothers who are depressed are at increased risk for major depression later in life. On the other hand, if mothers are treated for depression, that increased risk disappears. The question is how to accomplish such a difficult task.

Deborah Kim, M.D., assistant professor of psychiatry and part of the Penn Center for Women’s Behavioral Wellness, is exploring two approaches at Penn. She set up a psychiatry office in an obstetrics clinic at HUP, where she and two psychiatry residents focus solely on pregnant patients one half-day per week. The need, she discovered, is overwhelming: She has a waiting list for her services of more than six weeks.

During her residency in psychiatry, Kim recalls, “we would see a lot of folks who come in pregnant or postpartum with depression, and no one knew what to do for them. They were getting a lot of misinformation in the community and often ended up hospitalized from being taken off their medications so quickly.” A clinic was originally started at a location among



other psychiatric services, but few women showed up. So Kim decided to start practicing inside the ob-gyn clinic where the depressed women already were.

Obstetrics professionals are already strapped for time even before having to provide mental-health treatment, and they are generally less comfortable in providing depression treatment than psychiatrists.

JOINING THE TEAM

C. Neill Epperson, M.D., widely known as an expert on women with depression, has joined Penn Medicine as director of the Penn Center for Women's Behavioral Wellness. The center, supported by the Department of Psychiatry, has sites at HUP and at Pennsylvania Hospital. It offers a range of therapeutic options, including psychotherapy, cognitive behavioral therapy, couples therapy, and psychopharmacology.



Epperson was recruited from Yale University, where she was director of the Yale Program for Women's Reproductive Behavioral Health. Her appointment at Yale was in the Department of Psychiatry and in the Department of Obstetrics, Gynecology, and Reproductive Sciences. In describing her research interests, Epperson notes that women experience major depression and panic disorder at twice the rate of men. In addition, women are particularly vulnerable at times of hormonal fluctuations – during menses, the postpartum period, and while going through the menopause transition. Epperson's primary research goal has been to illuminate the neuroendocrine contribution to psychiatric disorders and substance abuse in women.

So Kim has found them to be enthusiastic about the new arrangement. In fact, they would welcome more people like her – a difficult request, because even some psychiatrists balk at providing care to pregnant women if they don't do it routinely.

So far, Kim has been impressed with the results at the clinic. "One of the most interesting things we are finding is that

In her 1999 article "Postpartum Major Depression: Detection and Treatment," in *American Family Physician*, Epperson wrote that "A simple screening instrument can be used to increase the detection of postpartum major depression." But she also noted that "The detection of PMD is often complicated by several factors."

Among her articles of note is one published in the *Journal of Clinical Psychiatry* (March 2004) evaluating the use of bright-light therapy to relieve depression during pregnancy. After 10 weeks of light therapy, the women exposed to the bright light showed a significantly beneficial effect, suggesting that this kind of therapy might be effective for pregnant women who do not take antidepressants.

In 1996, Epperson published in the journal *Pharmacology, Biochemistry and Behavior* neuroimaging findings suggesting that brain concentrations of a neurochemical known as gamma-aminobutyric acid are altered in postpartum women and may contribute to risk for depression in that context.

Epperson earned her medical degree from the University of North Carolina at Chapel Hill and did her training at Yale. The recipient of a NARSAD Young Investigator Award in 1995, she received a NARSAD Independent Investigator Award 10 years later.

– John Shea

the women's partners are more accepting of treatment than the women think they will be."

The clinic has been so successful that another psychiatry clinic for pregnant and postpartum women with mental-health problems is scheduled to open in the ob-gyn clinic at 3701 Market Street in the spring.

Still, Kim acknowledges many challenges. "We're fighting stigma, the idea many people still believe that pregnancy is a time where a woman is supposed to feel really good but in reality women often don't." She also mentions a recent article in *Vogue* that repeated the old view that women should not take medications during pregnancy.

Kim has found that many providers are not comfortable working with pregnant women because they say there is not enough data. "Patients frequently tell us they had trouble finding someone to treat them," says Kim. She is proud that her clinic is driven by evidence-based treatments.

Kim concedes that there are "no perfect data" about treating women with depression during pregnancy and postpartum. But she cites a large amount of data that supports using various medications during pregnancy, as well as data showing the harm done when women are not treated. "To say you shouldn't treat is unethical," she asserts.

Some women, however, may still be uncomfortable taking medications during pregnancy. So Kim is also exploring Transcranial Magnetic Stimulation (TMS), a treatment approved by the FDA for recurrent major depression in the general population. The therapy uses magnetic fields to induce electrical currents in the brain; it does not require anesthesia and, unlike electroconvulsive therapy, does not induce seizures. If TMS is found to be safe and effective in pregnancy, women who refuse depression medications while pregnant may have another option. Because

TMS may be given by a nurse or trained technician, the limited number of psychiatrists would not be so important a factor.

So far, only four patients have been treated with TMS. Results are promising: three out of four women have responded to treatment, with no serious side effects to the women or fetuses. Kim presented results at the American Psychiatric Association poster session in May. Once Kim and her colleagues have treated more patients with TMS, they intend to publish the results formally.

Although some of Wheeler's Medicaid patients at the Dickens clinic do make their way to Kim's clinic, Wheeler believes more of her patients would receive mental-health care if she, too, had a psychiatrist on her floor. Then they would witness the trusting relationship between the psychiatrist and ob-gyn doctors and be able to set up appointments simultaneously. Another advantage would be that the wait list would be more manageable without having multiple clinics feeding into one office. For her part, Kim is optimistic that, given the good results of her clinic and the increasing awareness of mental-health concerns during pregnancy, more offices like hers will soon be appearing.

James P. Guevara M.D., M.P.H., a pediatrician at CHOP and associate professor of pediatrics at Penn, has been treating children for years. Along with his peers, however, he expresses uncertainty about how to treat the children's *mothers* with depression.

Traditionally, he says, pediatricians have not considered parents as within the scope of their practices. "But there is data on the effects of parental issues like depression on a child's well being." While he notes that "there's still not a lot of understanding of what to do," he believes the older view is changing.

Pediatricians keep no files on parents, are not paid for treating parents – and have no time to treat parents. Guevara tried screening parents and referring



"Many people don't perceive their emotions as something medicine can help with," says Ian Bennett, M.D., Ph.D.

them for mental- health treatment, but the parents did not go. So instead of focusing on how to treat the mothers, Guevara asked a different question: why was the mother's depression having such an impact on the children?

What he found was that parents often have dysfunctional parenting styles when they are depressed. They may overreact emotionally to their children. The children, in turn, fail to learn good attachment skills or how to modulate their own behavior. Then the children are at risk of repeating the same patterns with their own children.

Guevara recently received a three-year grant to take a parenting education class – one that has been successful in educating the general public about parenting – and adapt it to focus on teaching depressed parents. Parents will be educated about depression, how it affects parenting and children, and how to address those challenges. The study will focus on poor urban areas that suffer from inadequate mental-health care; one likely site is Penn's own neighborhood, West Philadelphia, where the majority population is African American.

Parents with multiple symptoms of depression will receive the telephone number of a mental-health agency that can help treat their depression as well as extra help in arranging the appointments. A trained social worker will deal with the barriers that keep them from their appointments – providing transportation, tokens, and child care. Half of the women will also be signed up for the parenting class.

Over time, says Guevara, his team hopes to see effects on the parents' parenting styles, level of stress, and social support. In particular, they will observe whether the interventions help them to build rapport with the other parents and learn skills that affect their children.

The class will meet for two hours once a week for three months. It will focus on parenting skills that are particularly challenging for a parent suffering from depression. In group discussions, parents will explain how they encourage their children. There will also be structured lessons on what commonly works for parents and specific approaches for making parenting positive.

If the study shows some benefits to the class, Guevara hopes that the Pennsylvania Department of Health or Medicaid might be interested in funding the intervention for a longer term. If that happens, commercial insurance companies would be more likely to fund it.

Despite the significant barriers, there has been much progress in mental-health care in recent times, and many health-care workers from several disciplines at Penn are continuing to advocate for creative solutions to a complicated problem. "I'm upbeat," says Wheeler. "I think we're going to change things." While she acknowledges the severely troubled economy of today, she nevertheless hopes that now is the time "when thoughtful people say what should happen and address how we can have mental-health care affordable for all." ♥

A Few Words About Tradition

Ernest F. Rosato, M.D. '62, G.M.E. '66, professor of surgery and former chief of the Division of Gastrointestinal Surgery, was the featured speaker at this year's White Coat Ceremony for the entering Class of 2013. Since 1985, he has received the William Inouye Award for teaching 16 times. It is selected each year by Penn's surgical chief residents. In 2008, he received the I. S. Ravdin Master Clinician Award, one of the Awards of Excellence that the School of Medicine presents to its outstanding faculty members. Rosato was introduced by Jon B. Morris, M.D., professor of surgery and associate dean for student affairs, who noted that Rosato recruited him to Penn nearly 20 years ago. Following are edited remarks Rosato delivered about Penn Med's traditions.

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Photographs by Daniel Burke

WELCOME TO THIS NEWEST CLASS OF THE OLDEST MEDICAL SCHOOL IN AMERICA.

Welcome from someone who has just completed his first year of his second half century at the school. Tradition is the theme of the day – the handing down of information, beliefs, and customs, by word of mouth or by example from one generation to another without a written instruction. This is not the formal history; this represents the stories that we tell one another when we gather at a later day and recount our common experience. It is what bonds us together in a shared remembrance.

Where did it all begin, this Pennsylvania tradition? Today's presentations will provide some of that history: John Morgan and William Shippen Jr., sons of Philadelphia who went abroad to study in Edinburgh, Scotland – hence the thistle in the School of Medicine emblem. How they returned to their city to found the first medical school in the American Colonies. That school has prospered under generations of leaders. You will see some of the list of these illustrious

names and their great accomplishments. Thomas Eakins's portrait of D. Hayes Agnew in the Agnew Clinic immortalizes the development of the Department of Surgery and heralds in the age of scientific advancement in medicine.

No one walks alone through the halls of the University of Pennsylvania; all are accompanied by the many portraits on the wall, the busts on the pedestals, and the



memorabilia in the display cases. They tell in passing the history of an institution that extends back more than 240 years.

Like you, I arrived here with my own traditions. I had good parents, a physician father, so that I knew something of a medical life. I was directed here, actually sent, by my professor and chair of Biology, Dr. Mark Bauer, a Jesuit priest with a Ph.D. degree from Princeton. He assured me that the tradition of learning here was best, and I never found cause to disagree. This school provided me with the education that made me a good physician in 1962. It provided me with the tradition of learning that I think has allowed me to remain a good physician in 2009.

Where did it all begin for me? It began with professors who were not yet pictures on the wall, nor names on buildings. They walked the halls in buildings which were named for their own predecessors. Let me tell you of a few.

Isidor Ravdin, whose picture hangs in the lobby of the main entrance to the hospital, the Ravdin Pavilion, was born in Indiana, came to medical school at

the University of Pennsylvania in 1916, and stayed for a long and productive life. He was chairman of Surgery from 1945 to 1960. He was a giant of his time with exceptional achievements in medicine, in the military in World War II, and in civic affairs. Rav, as his friends and admirers called him, had a vibrant personality and a love for all people great and small. He could be a demanding man, sometimes harsh, sometimes paternalistic, as was characteristic of surgery in the day. He was demanding but forgiving. For example, if you somehow failed to measure up, he would fire you. "You're fired," he would say, and there was no appeal. You simply left for a few hours, and then you returned. The matter would not be mentioned again. Point made – and received.

For all of that paternalism and brusqueness, everyone loved Rav because he loved his students and believed in them. The best illustration of this was his own surgery. Dr. Jonathan Rhoads relates the story in his memoirs. Dr. Ravdin had developed cholecystitis and needed gallbladder surgery. Dr. Alan O. Whipple came down from New York and Dr. Eldridge Eliason, the Chairman of Surgery here, was also in attendance. Dr. Rhoads went to pick up Betty Ravdin, thinking his role to be social support, but was told on arrival that Rav had said he was to do the surgery and Whipple would assist. Dr. Rhoads was two years out of his training.

Ravdin believed in his students. He was devoted to research and education. He spurred the surgical community to embrace the scholarly life. This was heady stuff for us youngsters who previously thought that physicians came from the debating societies and surgeons from the rugby field. But if you were to run with Rav, you had to be something more. Dr. Rhoads again: "Dr. Ravdin was at his best as a developer of young people. His vision of what they could accomplish was generally more optimistic than their own; and



with his encouragement they often rose to his expectations rather than be limited by their own narrow horizons."

Julian Johnson was the first Professor of Cardiothoracic Surgery here. His portrait is in the anteroom outside Medical Alumni Hall in the Maloney Building. He is in surgical garb and his steely resolve is obvious. He had an intensity in patient care that was surely fueled by the frequent failures encountered during those pioneer days of heart surgery. He drove himself and he drove his protégés very hard. Many found him too hard, but he also had many admirers, and I was one of them. He told me once that he never was hard on someone who had made a mistake. They would be hard enough on themselves and needed support rather than further criticism. It was failure of effort and dedication that drew his ire. When someone recognized you for an accomplishment, he would say, "I taught him everything he knows" if he concurred with the compliment. Once shortly before his death, he shared a hospital room with my patient scheduled for surgery the following day. After we exchanged pleasantries, Dr. Johnson told my patient that he need have no concerns because "I taught him everything

he knows." Dr. Johnson was dying and he knew it, and yet he could reach out to comfort his roommate and to provide for me his final assessment that he was satisfied with how I had turned out. That was the last time that I saw him. I recall he told me that we don't always recognize our best teachers in the event but only with the passage of time. The best are not always the easiest, and they always push you to excel.

I have singled out these two because of my relationship with them in my earliest years – years most similar to your present style of life. I have not tried to encompass Dr. Jonathan Rhoads, whose portrait hangs on the wall of the Rhoads Pavilion and who guided my surgical life for 40 years as mentor and colleague. I can only urge you to read about him. He was a most extraordinary man.

Tradition – the oral telling from one generation to the next. When we older surgeons gather, we still speak of these men, tell stories about them, and they live in us because they have changed our hearts and souls. When we are gone, they will retreat back on to the walls, brought out only on great occasions such as this. Their stories will be replaced by stories about others – the Department under Dr. Barker, Dr. Kaiser, and now Dr. Drebin, yes, and hopefully stories about me.

And that will be pleasing because stories about me reflect what I have learned from these men and the countless others who have been here for the past 50 years. Rosato stories do abound. But it is not Rosato lore, it is the lore of this University. This is the essence of tradition. We take the story, we bring it into ourselves, and then we pass it along in one continuing spirit, the tradition of medicine at the University of Pennsylvania. For you, it begins today. You will hear the story, you will bend it, you will pass it on. You will indeed be a physician – and something more. ■



Development Matters

THANKS, ALUMNI! YOU HELP MAKE PENN



Our alumni, faculty, and students take enormous pride in the School of Medicine and its ability to change lives. It is why, this year, 2,562 alumni from classes spanning more than 70 years have demonstrated their support for our important work.

Annual gifts make it possible for the School of Medicine to provide scholarships, enhance facilities, and develop new academic programs. These gifts also help Penn Medicine remain a leader in research and patient care.

Here, we recognize the Penn Medicine members of the **Benjamin Franklin Society**: the University's prestigious leadership giving society. These medical school and graduate medical alumni have supported the School of Medicine with gifts of \$2,500 or more. Names marked with a "T" are also members of the **Thistle Society**, whose members give in three consecutive years' persons marked with an "*" are deceased. View a full list of alumni donors at www.med.upenn.edu/alumni.

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Wolfram Rieger, M.D., G.M.E. '86
T Rhoda Rosen, M.D. '58

An Inspiration for Young Alumni

Julie Linton, M.D. '07, truly knows the benefit of a helping hand – and can't wait for her opportunity to help future generations of medical students. Julie received full tuition in Penn's School of Medicine for all four years through the Twenty-First Century Endowed Scholars program, launched with an exemplary leadership gift from Walter Gamble, M.D. '57, and his wife, Anne.

Now a third-year resident at The Children's Hospital of Philadelphia, Julie is committed to supporting Penn Medicine. She is a member of the Thistle Society, giving to scholarship support through the annual fund for the past three years.

Julie's generosity also extends beyond University City. Before beginning her studies at Penn Medicine, she spent nine months on a Fulbright grant in Panama and was part of the leadership team for a global health initiative at CHOP. She says, "Providing care in a severely resource-limited setting forces me to remain mindful of our many privileges in the United States, and to appreciate the capacity to find joy in simplicity and genuine human connection."



Linton

Tommy Leonard

To learn more about supporting your medical alma mater, visit <http://www.med.upenn.edu/alumni/>

- T Frederic Goodman Sanford, M.D. '66
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- T Neil Steven Silverman, M.D. '84
- T Matthew B. Stern, M.D., G.M.E. '82
- T Brian L. Strom M.D., M.P.H.
- T Carol Herman Szarko, M.D. '66, G.M.E. '69
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- T Robert E. Weibel, M.D. '55

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- T R. Nick Bryan, M.D., Ph.D.
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- Howard Paul Furst, M.D., G.M.E. '00
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- W. Darby Glenn III, M.D. '56
- T Allan M. Greenspan, M.D. '73, G.M.E. '79

T = Thistle Society member, * = deceased
View a full list of alumni donors at www.med.upenn.edu/alumni

An Urgent Charge: Redesigning the Medical Campus

The new top priority of Penn Medicine's "Making History" campaign is the renovation and revitalization of the School of Medicine's physical campus. These new spaces are needed to better support Penn's renowned curriculum and ensure that Penn remains competitive among our peer schools.

In addition to new flexible classrooms, the redesigned medical education space includes tentative plans for a transformed Biomedical Library as well as a bright and vibrant common area located along Hamilton Walk. The design also envisions students enjoying multiple student lounges and relaxed study areas.

The new space will allow students to transition easily from team study to individual study – and by coupling it with state-of-the-art digital media and upgraded, wireless technology, medical students will be able to:

- collaborate with students and researchers worldwide
- create, publish, and share case-based presentations and other multimedia creations
- take differential diagnosis to a new level with interactive multimedia presentations, instant polling technology, and instant access to online resources



A look north through the connector to Hamilton Walk. All the new facilities will be closely integrated with other health-care buildings, bringing together the spectrum of research and clinical experience.

Your support is crucial – financing for this project will rely entirely on philanthropy. It so important that all of our alumni be involved in this new phase in the history of the School of Medicine. Take this special opportunity to make a meaningful impact for the students, faculty, and patients of Penn Medicine.

To learn more about the new School of Medicine education space, contact Vanessa Marinari at (215) 898-5164 or marinari@upenn.edu, or visit www.med.upenn.edu.

- T Robert L. Hall, M.D. '53
- T Richard W. Hazen, M.D. '58
- T M. Stephen Heilman, M.D. '59
- T Rima Herold Himelstein, M.D. '86
- T Douglas G. Jacobs, M.D. '71, G.M.E. '72
- T Peter J. Jannetta, M.D. '57, G.M.E. '64
- T Ralph A. Jessar, M.D. '46, G.M.E. '50
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- T Martin S. Kanovsky, M.D. '78, G.M.E. '79
- T Lawrence A. Kerson, M.D. '68
- T Sami L. Khella, M.D. '84, G.M.E. '89
- T John B. Kucharczuk, M.D. '51, G.M.E. '58
- T Larry C. Kuo, M.D. '78
- T Robert J. Laskowski, M.D. '78
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- T Paul Miller, M.D. '43
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- T Nicholas E. Mischler, M.D. '70
- T Raman L. Mitra, M.D. '85, G.M.E. '89
- T Grant Morrow, M.D. '59, G.M.E. '63
- T Philip K. Nelson, M.D. '52, G.M.E. '58
- T David Norman, M.D. '67, G.M.E. '71
- T C. Lowell Parsons, G.M.E. '77
- T Debra Jo Kern Pennington, M.D. '88
- T Frederick L. Porkolab, M.D. '72, G.M.E. '78
- T Jules B. Puschett, M.D. '59
- T Stephen A. Rafelson, M.D. '72
- T Kenneth A. Richman, M.D. '74, G.M.E. '79
- T John A. Schmidt Jr., M.D. '76
- T George W. Schnetzer III, M.D. '64
- T William G. Sharrar, M.D. '66
- T Roberta J. Smith, M.D. '68
- T Eric A. Strom, M.D. '72
- T Robert M. Wachter, M.D. '83
- T Rita Marie Watson, M.D., G.M.E. '79
- T Franklin H. West, M.D. '45 G.M.E. '51
- T Estate of Edwin B. Wilson Jr., M.D. '45
- T Francis Wren, M.D. '98

Recent Gifts

The **Marian S. Ware Charitable Giving Fund** continues to support the vital work of the Marian S. Ware Alzheimer Program at Penn Medicine and the School of Nursing with a \$4.6 million grant. This three-year grant – recommended by the late Mrs. Ware's four children, the Honorable Marilyn Ware, Carol Ware Gates, Paul W. Ware, and John H. Ware IV – will support coordinated drug discovery efforts, research designed to improve participation in clinical trials, quality-of-life assessments, a study of stress-related biomarkers, and research into nursing continuity of care.

Marjorie G. Ernest, CW '56, has generously named the University the beneficiary of her estate. More than \$3 million of the funds from the estate of Miss Ernest and the **Estate of Richard B. Ernest, C '13, M.D. '15**, will support the Department of Orthopaedic Surgery, two scholarship funds at the School of Medicine, and a scholarship fund at Penn's School of Arts and Sciences.

The **Mark H. & Blanche M. Harrington Foundation**, a long-time supporter of clinical cancer research in the Department of Surgery, has recently made an extremely generous leadership gift of \$1.0 million to help establish the Rhoads–Harrington Professorship in the Department of Surgery.

*To make a gift to Penn Medicine, or for more information, please contact the **Office of Development and Alumni Relations**, 3535 Market Street, Suite 750, Philadelphia, PA 19104-3309, or call 215-898-0578.*

Making History: Every Gift Matters

Thanks to your many generous contributions to our “Making History” campaign, we have raised approximately \$714 million to address the most pressing medical challenges of our time. *All of us at Penn Medicine deeply appreciate your continued support and loyalty.*

Visit the campaign Web site at www.makinghistory.upenn.edu to learn more.





Progress Notes

Send your progress notes to:

Andrea Pesce
Assistant Development Officer
PENN Medicine Development
and Alumni Relations
3535 Market Street, Suite 750
Philadelphia, PA 19104-3309

'50s

Rody P. Cox, M.D. '52, G.M. '56, was awarded a Mastership in the American College of Physicians at its convocation in Philadelphia in April. He was cited for his research on molecular and genetic studies of mitochondrial multi-enzyme complexes and their role in human diseases. He has also received many teaching awards for integrating molecular biology into clinical medicine. Cox is a professor of internal medicine at the University of Texas Southwestern Medical Center and former dean of its medical school.

Peter J. Jannetta, M.D. '57, G.M.E. '64, vice chairman of the Department of Neurosurgery at Allegheny General Hospital in Pittsburgh, has received the Medal of Honor from the World Federation of Neurosurgical Societies. He was honored for his important contributions to the advancement of medicine, including his groundbreaking research into the pathology and treatment of cranial nerve compression syndromes. Jannetta developed a microvascular decompression procedure that became the standard of surgical care for relieving the excruciating facial pain involving the trigeminal nerve.

'60s

Allen D. Roses, M.D. '67, G.M.E. '71, recently returned to the Duke University School of Medicine to lead a new drug discovery institute. One of the world's leading investigators of Alzheimer's disease, Roses left Duke in 1997 to become senior vice president for genetics research and pharmacogenetics at GlaxoSmithKline. The focus of the new institute is to translate published research into therapeutic molecules by tak-

ing on a role that has traditionally been held by the pharmaceutical and biotech industries. The institute's scientists will also begin to investigate potentially successful molecules that have cleared preclinical safety studies but have been passed over for further development by medium and large pharmaceutical companies. Roses has reassumed his chair as the Jefferson-Pilot Professor of Neurobiology and Genetics and is a member of the Duke Institute for Genome Sciences & Policy.

Doris G. Bartuska, M.D., G.M.E. '68, was named a Master of the American College of Endocrinology, an honor bestowed on only one, two, or three physicians a year. She is an emeritus professor of medicine at Drexel University School of Medicine, formerly the Medical College of Pennsylvania. A former director of the Division of Endocrinology, Diabetes, and Metabolism and of the fellowship training program at the Medical College of Pennsylvania, she also served as president of its medical staff. In 2008, she received the Pennsylvania Medical Society's Distinguished Service Award.

Patricia A. Gabow, M.D. '69, chief executive officer of Denver Health, received an honorary degree in May from the University of Colorado Board of Regents in recognition of her longstanding contributions in leading Denver Health and making it one of the nation's model integrated health-care delivery systems and safety-net hospitals. Gabow is a longtime member of the Department of Medicine of the University of Colorado at Denver.

'70s

Saul P. Greenfield, M.D. '77, is president-elect of the Society for Pediatric Urology. Director of pediatric urology at the Women & Children's Hospital of Buffalo, he is also a clinical professor of urology at the State of New York at Buffalo School of Medicine. He is author and co-author of more than 100 scientific articles and book chapters and is principal investigator for a clinical trial for children with vesicoureteral reflux, sponsored by the N.I.H. He is a former president of the Amer-

ican Association of Pediatric Urologists and is a member of the executive committee of the Urology Section of the American Academy of Pediatrics.

Nicole Lurie, M.D. '79, M.S.P.H., was nominated by President Barack Obama to be Assistant Secretary for Preparedness and Response in the Department of Health and Human Services. She is senior natural scientist and the Paul O'Neil Alcoa Professor of Policy Analysis at the RAND Corporation. As co-director of the RAND Center for Domestic and International Health Security, she has led RAND's work in public health and preparedness. In May, she received the Distinguished Graduate Award, the highest honor of Penn's School of Medicine.

Alan M. Sooho, M.D., G.M.E. '79, M.B.A., retired in July after 31 years with the Department of Veterans Affairs. For the last 12 years, he was chief of staff at the VA Medical Center of Battle Creek, Michigan. He plans to return home to Massachusetts.

'80s

William D. Ju, M.D. '82, G.M.E. '87, was recently appointed president and chief executive officer of Follica, Inc. Focused on dermatology and stem cell tissue re-engineering, Follica is based primarily on the work of George Cotsarelis, M.D. '87, the Albert M. Kligman Associate Professor of Dermatology at Penn's School of Medicine.

Lewis Wetstein, M.D., G.M.E. '82, was recently elected president of the New Jersey Chapter of the American College of Surgeons. He serves as chief of thoracic surgery at Community Medical Center in Toms River, N.J., and chief of surgery and secretary/treasurer of the medical staff at Kimball Medical Center in Lakewood. In addition to his surgical practice, he has been a member of the Air Force Reserves/New Jersey National Guard for more than 33 years. He served as commander of the 514th Air Medical Squadron at McGuire Air Force Base, N.J., and will retire this year from his position as State Air Surgeon of the New Jersey Air National Guard.

Wetstein is associate clinical professor of surgery at both the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School and the Uniformed Services University of the Health Sciences in Bethesda, Md. He serves as president of the Society of Surgeons of New Jersey.

Harry L. Leider, M.D. '83, was elected president and chairman of the board of the American College of Physician Executives, a national organization of more than 10,000 physicians. A member of the College for 20 years, he has served as a core faculty member there while teaching courses on improving the quality of health care. Leider is currently the chief medical officer and senior vice president of Ameritox, which has headquarters in Baltimore. It monitors pain prescription regimens.

Louis M. Bell Jr., M.D., G.M.E. '85, received the Lindback Award for Distinguished Teaching at the University of Pennsylvania. Dr. Bell is a professor of pediatrics in the School of Medicine and chief of general pediatrics at The Children's Hospital of Philadelphia.

G. David Elkin, MD. '85 is a consultation-liaison psychiatrist at San Francisco General Hospital, where he co-directs medical-student education. He recently received the Osler Award, a lifetime-teaching award from the graduating class of the University of California at San Francisco. He serves on the hospital ethics committee and leads efforts to bring the humanities to medical student and resident training.

Walter J. Curran, M.D., G.M.E. '86, a Georgia Cancer Coalition Distinguished Scholar, has been named executive director of the Emory Winship Cancer Institute. Curran, who joined Emory University in January 2008, has served as the Lawrence W. Davis Professor and Chairman of Emory's Department of Radiation Oncology and as chief medical officer of Emory Winship. He is group chairman and principal investigator of the Radiation Therapy Oncology Group, a cooperative group funded by the National Cancer Institute. Emory Winship announced its N.C.I. designation

earlier this year, becoming the first facility in Georgia to earn this designation. A Fellow in the American College of Radiology, Curran has led several landmark clinical and translational trials in both areas and is responsible for defining a universally adopted staging system for patients with malignant glioma.

'90s

Aaron E. Carroll, M.D. '98, is the author, with Dr. Rachel Vreeman, of *Don't Swallow Your Gum!: Myths, Half-Truths, and Outright Lies About Your Body and Health* (St. Martin's Press, 2009). Carroll is an assistant professor of pediatrics in the Children's Health Services Research Program at the Indiana University School of Medicine and director of the Center for Health Policy and Professionalism Research. His current research interests include the use of technology in health care, decision analysis and cost-effectiveness analysis, and health policy and professionalism.

Vicente H. Gracias, M.D., G.M.E. '99, who had been associate professor of surgery in Penn's Division of Traumatology and Surgical Critical Care, has joined the Robert Wood Johnson Medical School in New Brunswick, N.J., as the founding chief of a new surgical division of trauma and surgical critical care. Formerly section chief of Surgical Critical Care, he received the Teacher of the Year award from the division in 2004. He is nationally recognized for teaching the technique of focused abdominal sonogram in trauma (FAST) and has developed an education exchange with Latin America.

'00s

Kevin J. Chang, M.D. '00, and his wife, **Rohini Nadgir**, M.D. '00, Sharon, Mass., had their first child, daughter Soniya Hui-Fen Chang, on June 13. Chang recently became a radiologist and full partner at Rhode Island Medical Imaging and currently serves as an assistant professor at the Brown University Alpert Medical School. Nadgir was recently promoted to

assistant professor at Boston University and practices neuroradiology at Boston Medical Center.

Andrew Jawa, M.D. '02, was appointed a surgeon of hands and upper extremities in the Department of Orthopaedic Surgery at Boston Medical Center and will be recommended for assistant professor of orthopaedic surgery at Boston University School of Medicine. He completed his residency in orthopaedic surgery at Harvard University as well as two fellowships at Massachusetts General Hospital. His clinical expertise is in shoulder reconstruction for instability, arthritis, trauma, nerve injury, and rotator cuff disease.

Rajiv Shah, M.D. '02, who became Under Secretary for Research, Education, and Economics in the United States Department of Agriculture earlier this year, has now been nominated by President Obama to be the next administrator of the United States Agency for International Development (USAID). The independent federal agency is responsible for most non-military foreign aid. Its goal is to help people overseas who are struggling to make a better life, to recover from a disaster, or to live in a free and democratic country. Earlier, Shah had been at the Bill and Melinda Gates Foundation, where he managed the Foundation's agricultural development program.

OBITUARIES

Samuel Baer, M.D. '33, Wyncote, Pa., a retired cardiologist and former chair of the medical board of Albert Einstein Medical Center; January 3, 2009. He had edited *Punch Bowl*, Penn's undergraduate humor magazine. He was 100 years old.

Charles William Mills, M.D. '38, Shoreline, Wash., an obstetrician-gynecologist who had maintained a practice in Salem; October 22, 2008. During World War II he served with the U.S. Army in Italy.

Benjamin Coleman, M.D., G.M. '39, West Caldwell, N. J., a retired otolaryngologist; April 24, 2002.

Arnoldus Goudsmit, M.D., Ph.D., G.M. '41, Rochester, N.Y., former chief of surgical oncology at the Veterans Administration Medical Center in Minneapolis and a founder of the American Society of Clinical Oncology; February 11, 2005. During World War II he was a medical officer with the U.S. Army Air Corps. He had taught at the University of Pennsylvania and the University of Pittsburgh. Goudsmit was the first president of the Ohio Chapter of the American Society of Internal Medicine.

Wilbur M. Lutz, M.D. '41, G.M. '47, Wernersville, Pa., November 4, 2008

Richard W. Rooker, M.D. '41, G.M. '47, Winona Lake, Ind.; a retired otorhinolaryngology surgeon; May 4, 2009. He was a captain in the Army in World War II, attached to the 543rd Engineer Boat and Shore Regiment, and served as a doctor in New Guinea, the Philippines, and occupied Japan. He was president of Niagara County Board of Health and of the medical staff of Memorial Hospital in Niagara Falls.

Maston K. Callison, M.D., G.M. '42, Memphis, retired dean of the University of Tennessee medical school; December 17, 2008. A captain in the U.S. Army Medical Corps during World War II, he became assistant chief medical officer of the American hospital in Berlin.

Rudolph E. Jacobi, M.D., G.M. '42, Katy, Texas, a former general practitioner; February 7, 2001.

E. Osborne Coates Jr., M.D. '43, G.M. '47, Topsham, Maine, the retired assistant medical director of a local veterans hospital; November 11, 2008.

Augustin T. Giordano, M.D. '43, Longport, N.J.; July 6, 2009. He did his training at Philadelphia General Hospital and maintained a pediatrics practice in Philadelphia for many years.

Leonard L. Malamut, MD. '43, Philadelphia, July 5, 2008. Before retiring in 1990, he practiced internal medicine and held an academic appointment at Temple University School of Medicine.

Thomas S. Royster Jr., M.D. '43, Vero Beach, Fla., a retired surgeon at Roosevelt Hospital in New York; August 4, 2008. He had served in the U.S. Army Medical Corps.

Dayton T. Kieswetter, M.D. '44, Santa Barbara, Calif.; January 4, 2009. At the beginning of World War II, he served in the Army Medical Corps as a physician at Walter Reed Hospital and was discharged in 1947 with the rank of captain. Kieswetter was president of the medical staff at the Hospital Center at Orange, an associate professor of medicine at the New Jersey College of Medicine, and a fellow of the American College of Physicians.

Ralph M. Weaver, M.D. '44, Butler, Pa., a retired pathologist; October 25, 2008. During World War II he was a medical officer with the U.S. Army's First Infantry Division in Europe. He practiced pathology for 35 years in South Carolina and Pennsylvania. He was founder and president of Laboratory Supply Corporation. With his wife, Sallie, he established and funded the Dr. Ralph and Sallie Weaver Professorship in Research Medicine at Penn.

William E. Evans, M.D. '45, State College, Pa., a retired physician who had maintained a practice in Crossville, Tenn.; December 29, 2008.

Mano Robert Golden, M.D. '45, Fort Washington, Pa., a urology surgeon and investor, July 21, 2009. At Penn, he went through the Navy's World War II program to train officers, then was a medical officer at a Navy facility in Batavia, N.Y. He interned at Albert Einstein Medical Center and completed a urological residency at Sinai Hospital in Baltimore. He had practices in Center City Philadelphia and Norristown. A former chief of urology at Montgomery Hospital and Sacred Heart Hospital in Norristown, he was on the staff of Presbyterian Hospital and served on Penn's medical faculty. He was a diplomate of the American Board of Urology. Golden pursued an interest in investing during his decades as a surgeon and, after retiring from medicine in 1991, turned full time to his invest-



ments. He shared his common-sense approach in his 1995 book, *Bulls, Bears, Sheep, and Eagles*.

Franklin C. Kelton, M.D. '45, Newtown Square, Pa., a retired physician; July 11, 2008. During World War II he served in the U.S. Army.

Earle B. Thompson, M.D. '45, Arvada, Colo., a retired physician; December 12, 2008.

John L. Cogland, M.D., G.M. '46, Paradise Valley, Ariz.; April 30, 2005. He had been chief of staff at both St. Joseph's Hospital and Good Samaritan Hospital in Phoenix.

Leon Eisenberg, M.D. '46, Cambridge, Mass., considered one of the nation's most influential child psychiatrists; September 15, 2009. He earned both his undergraduate and medical degrees from the University of Pennsylvania. Although he graduated as valedictorian of his medical class, he was denied an internship at HUP. Instead, he went to Mt. Sinai Hospital in New York, where he was drawn to psychiatry. After completing his residency in psychiatry at Sheppard Pratt Hospital in Towson, Md., he spent two years in the Army, teaching psychiatry. Then in 1952, he began a residency in child psychiatry at Johns Hopkins, working with Dr. Leo Kanner, who first described autistic behavior. Together, they completed the first detailed, long-term study of children with autism. In the 1960s, Eisenberg performed the first randomized, placebo-controlled clinical trials of drugs given to children identified as "delinquent" or "kinetic." Those studies became the basis for the drug treatment of what is now called attention deficit disorder. Eisenberg is credited with clarifying the important relationship between the biological and the social. In 1967, he became chief of psychiatry at Massachusetts General Hospital and soon became involved in developing the affirmative action program at Harvard Medical School. In 1980, Eisenberg was invited by the dean of Harvard's medical school to establish the Department of Social Medicine (recently renamed the Department of Global Health and Social Medicine). Among the

department's aims is applying the tools of social science to improving access to and the practice of medicine to a wider population. According to Arthur Kleinman, a professor at Harvard University, "Leon Eisenberg is one of the seminal figures in American medicine and in psychiatry of the past half century."

Warren W. Hampe Jr., M.D. '46, Haverford, Pa., a retired psychoanalyst and former teacher of psychiatry at Temple University; January 28, 2009. A polio survivor, he had served at the U.S. Army Hospital in Fort Jay, N.Y., treating World War II veterans suffering from post-traumatic stress disorder.

Joseph J. Kline, M.D., G.M. '46, Jupiter, Fla., a retired pediatrician; March 31, 2009. He served on the staff of the Capital Health System and later became medical director of the children's unit at the Trenton Psychiatric Hospital. He was a former president of the Medical Society of New Jersey.

Elwood Troyer Hansen, M.D., G.M.E. '46, Laguna Woods, Calif., a retired pediatrician; November 3, 2005.

George L. Brown Jr., M.D., G.M. '47, Lancaster, Pa., a retired dermatologist; November 23, 2008. He had a private practice in Abington from 1952 to 1978. During this time, he served on the staff of several local hospitals and was chief of staff for dermatology at Abington Memorial Hospital. He retired to Lancaster in 1978.

Joseph C. Furnary, M.D., G.M. '47, Annapolis, Md., a retired radiologist; July 11, 2003.

Samuel E. Greenspon, M.D., G.M.E. '47, Wyncote, Pa., a retired anesthesiologist; September 5, 2008.

Leland R. House, M.D., G.M. '47, Monterey Park, Calif., a retired otolaryngologist; October 5, 2003.

Edmond Preston III, M.D. '47, G.M. '51, Medford, N.J., a retired pediatrician; October 29, 2008. He had worked at Burlington County Memorial Hospital.

Frank M. Melton, M.D., G.M.E. '48, Wilmington, Del., a retired dermatologist; January 1, 2005.

Paul W. Burlison, M.D., G.M. '49, Naples, Fla., a former internist; December 19, 2005. He was on the faculty of the University of Alabama School of Medicine for more than 30 years. In 1998, he received the Garber-Galbraith Medical-Political Service Award for outstanding service to the medical profession. The Alabama Medical Association endowed an award in his honor.

George W. Dorman, M.D., G.M.E. '49, Prescott, Ariz., a retired chief of surgical services at the Children's Medical Center of Dallas; October 1, 2008.

Cornelius E. McCole, M.D. '49, Detroit, emeritus chair of ophthalmology at the Henry Ford Health System; June 19, 2008.

Henry D. McIntosh, M.D. '50, Lakeland, Fla., a retired physician and past president of the American College of Cardiology; December 26, 2008. For his service in the U.S. Parachute Infantry during World War II, he was awarded a Silver Star, a Croix de Guerre, and two Bronze Stars.

John D. Anderson III, M.D. '51, Wellsboro, Pa., a retired anesthesiologist who practiced at Hahnemann and Bryn Mawr hospitals; December 29, 2008. During World War II he was a private in the U.S. Army's 9th Infantry Division, 39th Regiment, in Europe, for which he received a Purple Heart and two Bronze Stars.

Harold O. Hallstrand, M.D., G.M. '51, Miami, a retired surgeon who had maintained a practice with his brother in Miami; October 11, 2006. He also taught at the University of Miami School of Medicine.

William I. Heine, M.D., G.M. '51, Elkins Park, Pa., a cardiologist; September 10, 2008.

Joseph C. Moore, M.D., G.M. '51, Summerville, S.C., a retired obstetrician and gynecologist; November 22, 2008. He practiced in Greenville, S.C., for many years.

Hilary W. Cholhan, M.D., G.M. '53, Brooklyn, N. Y., a retired obstetrician and gynecologist; February 12, 2004.

Robert Shaw, M.D. '53, Bolinas, Calif.; March 26, 2009. He served as director of family and children's mental health services for the City of Berkeley and was a visiting professor at the Lawrence Berkeley Laboratory. He established The Family Institute of Berkeley, a teaching institute for psychiatrists and other physicians and health workers. Shaw was the author of *The Epidemic: The Rot of American Culture, Absentee and Permissive Parenting, and the Resultant Plague of Joyless, Selfish Children* (Harper, 2003).

Howard K. Clough, M.D., G.M. '54, Berwyn, Pa., a former ophthalmologist; September 26, 2006. He was on the medical staff of Wills Eye Hospital and Lan-kenau Hospital for more than 40 years. A member of the board of Hahnemann Hospital, he was the medical director for CrossWorld Ministries in Bala Cynwyd. He also served as the team ophthalmologist for the Philadelphia Flyers 1974-1975.

Charles F. Whitten, M.D., G.M. '54, Detroit, a semi-retired pediatrician; August 14, 2008. He was the associate dean for curricular affairs and a distinguished professor of pediatrics at the Wayne State University School of Medicine and had been associate dean for special programs. He was chair of the advisory committee of the Michigan Department of Public Health, the Genetic Disease Committee, and the Task Force on Infant Mortality. He was also co-chair of the Expert Committee on AIDS. Whitten also served on committees of the American Academy of Pediatrics, the National Academy of Science, and the National Institutes of Health.

Venustiano H. Borromeo, M.D., G.M. '55, East Greenbush, N.Y.; July 23, 2004.

Anthony J. Digiovanni, M.D., G.M.E. '55, San Antonio, Texas; May 11, 2006. After his residency in anesthesiology, he returned to active duty in the United States military with assignments in England, Florida, and finally in San Antonio, at the Wilford Hall

United States Air Force Medical Center. There he served as chief of the anesthesiology services and director of residency training. After retiring in 1970, he joined the staff of the Santa Rosa Medical Center and the faculty of the University of Texas School of Medicine as a clinical professor of anesthesiology.

Robert B. G. Dorsen, M.D., G.M.E. '55, Sarasota, Fla.; April 9, 2009. He had served as chief of obstetrics and gynecology at the United States Public Health Service hospitals in Staten Island, N.Y., and in New Orleans. He then became deputy director at the Albert Einstein College of Medicine, N.Y., and spent eight years in private practice in New York. He was a fellow of the American College of Surgeons and of the American College of Obstetrics and Gynecology. After retiring from medicine, Dorsen went full time into the theater and appeared in 14 films, including *Tootsie*, as well as in soap operas such as *One Life to Live*. He also performed off Broadway in *Little Murders*.

Pierre R. Grondin, M.D., G.M. '55, Shawinigan, Quebec, a retired surgeon; January 10, 2006. He was the former head of cardiovascular surgery at the Montreal Heart Institute and St. Francis Hospital in Miami Beach. He was named an Officer of the Order of Canada for his contribution to the advancement of thoracic and cardiovascular surgery.

Irwin Kantor, M.D., G.M. '56, Summit, N.J., a retired clinical professor of dermatology at Mt. Sinai School of Medicine; February 2, 2009.

Milton M. Connell, M.D. '57, G.M. '64, Phoenix, a retired ophthalmologist; September 28, 2008.

Harry K. Ziel, M.D. '57, G.M.E. '61, Glendale, Calif., a retired obstetrician and gynecologist; March 22, 2009. Known for his landmark medical discovery of the link between estrogen and the risk of endometrial cancer, Ziel was emeritus clinical associate professor of obstetrics and gynecology at the Keck School of Medicine at the University of South California. In 2001, he

received the Teacher of the Year award from the Los Angeles Ob/Gyn Society. His published essays include "How to Evaluate New Medical Discoveries," which appeared in *Skeptical* (1999).

Bao Jen Jing, M.D., G.M. '58, Bellaire, Tex., a former obstetrician and gynecologist; March 24, 2009.

David C. Northcross Jr., M.D., G.M. '58, Detroit, retired director of Mercy General Hospital, the first African American-owned proprietary hospital in Detroit, which had been founded by his parents in 1916; January 12, 2009.

H. Craig Whitaker, M.D. '58, G.M.E. '64, Wallingford, Pa., January 8, 2009. He took his internship at Womack Army Hospital at Fort Bragg, N.C. An obstetrician-gynecologist for 35 years, he was associated with Crozer-Chester Medical Center, where he was director of outpatient gynecological services. He received the Teaching Attending Award in 1994.

William P. Graham III, M.D. '59, G.M. '78, Thomasville, Pa., a retired professor of surgery and chief of plastic and reconstructive surgery at Penn State University; October 7, 2006.

William C. Hendricks Jr., M.D. '59, Jupiter, Fla.; March 28, 2009. He served as chief of the division of neurosurgery at Hamot Hospital in Erie, Pa., from 1978 to 1981, and for many years was medical director to the local multiple sclerosis society.

Murphy Townsend Scurry, M.D., G.M.E. '59, Galveston, Texas, a retired endocrinologist; April 21, 2009. He served in the U.S. Army at Walter Reed Institute from 1963 through 1966. Returning to Galveston in 1966, he was on the faculty of the University of Texas Medical Branch until 1981. He maintained a private practice until 1993, when he retired.

Dana N. Weeder, M.D. '59, New Castle, Del., a surgeon with the Exeter Clinic in Pennsylvania for 30 years; October 28, 2008. During his service in the U.S. Navy, he founded a field hospital in Chu Lai, Vietnam.

Joseph H. Calhoun, M.D. '62, G.M.E. '66, Haverford, Pa., former director of pediatric ophthalmology at Wills Eye Hospital; November 17, 2008. He was also on the staff of Bryn Mawr Hospital and maintained practices in Philadelphia and King of Prussia before retiring in 2007. For nearly 20 years, he volunteered with Project Orbis, treating children and health-care professionals in developing countries. In 2000, he received the Silver Tray Award from Wills, cited for his caring and modesty. A former president of the American Association of Pediatric Ophthalmology, he was co-author of *A Child's Eyes*, selected as the best medical book of 1999 by the American Medical Writers' Association.

William J. Medicott, M.D., G.M. '62, Port Townsend, Wash., former chair of orthopaedics at St. Luke's Hospital in Kansas City, Mo.; December 21, 2008.

Sol Browdy, M.D., G.M.E. '63, Park City, Utah, a former pediatrician; November 22, 2008. He practiced in Trenton, N.J., for 30 years and wrote several books, including *Life the Second Time Around: A Memoir* (2002).

Tomas F. Contreras, M.D., G.M. '63, Mount Laurel, N.J., a former surgeon and obstetrician/gynecologist; April 27, 2009. A founding member of the Philippine-American Medical Society of New Jersey, he was also a fellow of the New Jersey Obstetrics and Gynecology Society, the American Society of Abdominal Surgeons, and the Academy of Medicine in New Jersey.

John W. Curtis, M.D., G.M.E. '65, Salinas, Calif., a former dermatologist; April 16, 2009. Curtis served in the United States Navy and retired with the rank of Commander. He did one tour of duty at the U.S. Naval Support Activity Station Hospital in Da Nang, Vietnam.

Earl H. Godfrey, M.D., G.M.E. '65, Spartanburg, S.C., a retired professor of neurology at the University of South Carolina; July 22, 2008.

Bernard Ackerman, M.D., G.M.E. '67, New York City, a founding figure in the field of dermatopathology; December 5, 2008. After earning his medical degree at Columbia University, he took his residency at Penn, then was hired by the University of Miami. In 1973, he joined the faculty of New York University Medical School, where he headed the Skin and Cancer Institute. His laboratory there was one of the first to screen for early signs of Kaposi's sarcoma. He founded the Ackerman Academy of Dermatopathology, now part of Dermopath Diagnostics. He trained a generation of dermatologists to use his diagnostic method on an 18-headed microscope, which allowed users to view slides of skin tissue from dozens of cases at a sitting. He published more than 700 papers and more than 60 books. In addition, he founded two professional journals, *The American Journal of Dermatopathology* and *Dermatopathology: Practical and Conceptual*. While in training at Penn, he worked at Holmesburg Prison, where inmates were paid to undergo medical tests of chemicals and cosmetics. The experience sparked his interest in medical ethics, and in later years he was very critical of the research done at Holmesburg. In 2003, he started a Web site to expose expert witnesses he considered unreliable. Recently, he expressed skepticism that exposure to sunlight causes melanoma.

Irwin B. Boruchow, M.D., G.M.E. '68, Highlands, N.C., a former surgeon; April 9, 2000. He practiced thoracic and cardiovascular surgery at St. Francis Hospital Cardiovascular Center, where he was a major developer of the Center's open heart surgery program and served as assistant director. He also consulted at the Miami Beach Community Hospital and the Miami Heart Institute and served on the teaching staff at Mount Sinai Medical Center.

Rear Adm. Robert F. Knouss, M.D. '70, Adelphi, Md., an assistant surgeon-general in the U.S. Public Health Service; July 10, 2007.



Sylvan B. Green, M.D., '72, Tucson, Ariz.; December 13, 2008. He was director of biometry and held the inaugural Linda McCartney Breast Cancer Endowed Chair in Biometry at the Arizona Cancer Center. He was also professor of epidemiology and biostatistics in the College of Public Health at the University of Arizona. A fellow of the American College of Epidemiology, he served as president of the Society for Clinical Trials in 1994-1995. Green was a retired officer in the U.S. Public Health Service Commissioned Corps.

Robert Burt, M.D., G.M.E. '79, Indianapolis, a former radiologist; October 13, 2003.

Philip D. Smithey, M.D., '80, Dallas, Texas; July 29, 2002.

James Edward Bross, M.D., G.M.E. '84, Danville, Pa., a specialist in infectious diseases; May 17, 2000.

Joanne E. Finley, M.D., G.M.E. '85, Baltimore, formerly the New Jersey commissioner of health (1974-82) and Maryland's deputy secretary of health (1983-84); October 15, 2008.

FACULTY DEATHS

John R. Brobeck, Ph.D., M.D., emeritus professor of physiology in the School of Medicine; March 6, 2009. He was chair of the Department of Physiology from 1952 to 1970 and was a professor until 1982. He was named the Herbert C. Rorer Professor in the Medical Sciences in 1970. As Penn's judicial administrator from 1989 to 1993, he oversaw the resolution of the "Water Buffalo" incident. Before coming to Penn, Brobeck served on the medical faculty at Yale University, where he earned his medical degree in 1943. From 1963 to 1972, he was the chairman of the editorial board of the journal *Physiological Reviews*. A former president of the American Physiological Society, he was a member of the National Academy of Science and had been a fellow of the American Academy of Arts and Sciences.

Philip J. Escoll, M.D., a retired psychoanalyst and clinical professor of psychiatry at the School of Medicine; June 21, 2009. He earned his medical degree from Jefferson Medical College, where he won the biochemistry and psychiatry prizes and was elected to the Alpha Omega Alpha Honor Medical Society. He joined Penn's clinical faculty in 1961 and helped establish the psychiatric clinic for older adolescents at HUP. A former chairman of the committee on clinical faculty at the hospital, he was also a training and supervising analyst at the Philadelphia Center for Psychoanalysis and a former president of the Philadelphia Psychoanalytic Association. He won several teaching awards at Penn, including the Robert Dunning Dripps Award for Excellence in Graduate Medical Education, and received the Practitioner of the Year Award from the Philadelphia Psychiatric Society. He retired in 2003.

Mano Robert Golden, M.D. See Class of 1945.

Sukhamay Lahiri, Ph.D., emeritus professor of physiology; May 2, 2009. Born in what is now Bangladesh, Lahiri earned his B.S., M.S., and Ph.D. degrees in physiology from Calcutta University. Later, he earned another Ph.D. degree from Oxford University. He came to the U.S. on a Fulbright Scholarship in 1965 and joined the Penn faculty in 1969 as an associate professor of environmental physiology. In the course of his research on high-altitude physiology and medicine, he took part in several expeditions to Mount Everest, including one in 1960 on which he accompanied Sir Edmund Hillary. An expert on hypoxia, Lahiri received two prestigious grants to support his research: the MERIT Award from the National Heart, Lung, and Blood Institute and the Humboldt Research Award for a Senior U.S. Scientist from the Alexander von Humboldt Foundation in Germany. He was a former president of the International Society for Arterial Chemoreception.



Dedicated Alumnus Makes Scholarship his Legacy



For Ralph Weaver, C '41, M.D. '44, every trip back to campus for Alumni Weekend was one well worth making, despite the nearly six-hour drive between his residence in Butler, Pa., and Philadelphia. Dr. Weaver's experiences as both an undergraduate and medical student left him with an enduring love for Penn Medicine and a respect for the importance of medical education. He enjoyed a distinguished career as a pathologist and was an emeritus faculty member with the Butler Memorial Hospital. He had also been founder and president of Laboratory Supply Corporation and LABSCAL. This May would have marked his 65th Reunion. Sadly, Dr. Weaver passed away last October, but his extraordinary dedication to his alma mater will have a profound effect on medical students for generations to come.

Dr. Weaver was a longtime champion for scholarships at the School of Medicine. Recognizing their importance in providing opportunity to the brightest and most diverse pool of students, he made the School a part of his estate planning. He knew an estate gift would allow him to have a substantial impact on students and would instill a legacy at Penn.

Having donated to the Medical Class of 1944 Scholarship for many years and having interacted with students whose lives were touched by his generosity, Dr. Weaver incorporated the fund as part of his estate gift. He also allocated a portion of his planned contribution to the 21st Century Medical Scholarship. Dr. Weaver already had a charitable gift annuity and designated that, upon his death, the remainder would establish the Ralph and Sallie Weaver Endowed Scholarship. Ultimately, he wanted his lifetime achievements and assets to benefit as many students as possible, and estate planning allowed him to do just that.

Dr. Weaver chose one of a multitude of creative gift opportunities that benefit both the School of 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., director of Planned Giving, at 215-898-9486 or you can e-mail her at cewan@upenn.edu. For more information, please visit the Web site at www.med.upenn.planyourlegacy.org.

The Case for Health Care Reform

Few initiatives in recent years have provoked the degree of interest and, at times, contentiousness as the Obama Administration's attempt to reform health care. The extreme response likely comes because health care reform means many different things to different people. As a physician, I believe that it is, first of all, a civic and ethical imperative: the primary goal should be to expand coverage for the millions of Americans who have either no health-insurance coverage or very little. According to a recent national survey of doctor's attitudes, "a large majority of respondents (78%) agreed that physicians have a professional obligation to address societal health policy issues. Majorities also agreed that every physician is professionally obligated to care for the uninsured or underinsured (73%)" (*The New England Journal of Medicine*, published on line, September 14, 2009). I am glad so many physicians share my belief – but I wish the figure were higher.

Asked whether they were willing to accept limits on reimbursement for expensive drugs and procedures for the sake of expanding access to basic health care, the percentage drops: 67% said yes in this case. That figure suggests that health care reform is a very complex matter, intertwined with issues like costs, social attitudes, role of government, fears of rationing, and many others.

Cost is one of the components of reform that we cannot avoid facing. The United States currently spends about \$2.5 trillion annually on health care services and products, more than 17 percent of the gross domestic product. But the country scores only average or lower on many health indicators, compared to other industrialized nations. Many of us in academic medicine believe that reducing costs in the way we do our work will allow us to direct those savings toward the expansion of coverage. We must become more efficient, providing a higher quality



of care for less. Nobody says such an approach will be easy.

One of the important items related to health care reform that has garnered less attention is the status of the National Institutes of Health. Its impact on health care is not always apparent to the general public – or to our elected representatives. According to an article in *PLoS ONE* (July 2009), the NIH funded 28 percent of U.S. articles on cardiovascular disease over a recent 11-year period, and those articles were more likely to be published in "high-impact journals." In less abstract terms, the authors quoted Elias Zerhouni, M.D., who recently stepped down as NIH director. He asserted that research on coronary artery disease had prevented one million early deaths "at a cost of supporting the NIH of \$3.70 per American per year." Yet the authors of the article point out that NIH budgets have stagnated or even declined in terms of purchasing power over the last several years.

Another recent article took a broader look at the NIH's impact. In *Proceedings of the National Academy of Sciences (PNAS)*, the authors claim that NIH research "is the primary source of new therapies and treatments for major chronic diseases, many of which were viewed as relatively untreatable in the 1950s" (July 7, 2009). They argue that its budget should be quadrupled.

In *The New England Journal of Medicine*, Francis Collins, M.D., the new director of the NIH, also mentions the "absolute flat nature of the budget for biomedical research" for a five-year period and sug-

gests that NIH has suffered a loss of almost 20 percent in purchasing power (October 1, 2009). That is why academic medical centers strongly favor a larger budget for the NIH and want Congress to support such measures. Fortunately, we have some strong supporters, such as Frank Pallone, Democrat of New Jersey, who chairs the health subcommittee of the House Energy and Commerce Committee. In a statement on November 13, 2008, he referred to the NIH as "America's leading medical research agency and the foremost biomedical research institute in the world. It is through the work of NIH that we are living longer and healthier lives and may someday soon find cures for the epidemics of our time like cancer and diabetes."

Our mission involves curing disease and saving lives, through biomedical research and through expert clinical work. But to be fair, what we do must be available to as many people as possible. In his address on September 9, President Obama pointed out that "everyone in this Congress gets affordable insurance. And it's time to give every American the same opportunity that we've given ourselves." The president also quoted the late Senator Ted Kennedy, who wrote: "At stake are not just the details of policy, but fundamental principles of social justice."

The medical profession, of course, has its own ethical standards that echo these concerns. We cannot live up to those high standards while overlooking the plight of so many less fortunate citizens – by some counts, as high as 47 million – who lack health care coverage.

Today, as Congress considers its health care bills, the conditions for wide-ranging reform may not be auspicious. Still, we owe it to our patients to make the best effort possible. And smaller steps are infinitely better than no steps at all. ♥

Arthur H. Rubenstein, M.B., B.Ch.
Executive Vice President of the University of Pennsylvania for the Health System;
Dean, School of Medicine

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s the national debate on health care re-
form continues, experts at Penn Medicine
have been following the issue closely. The
CEO of Penn’s Health System discusses re-
form’s likely impact on academic medical
centers – and beyond. Faculty members
engaged in comparative effectiveness re-
search explain what part CER can play in
reforming health care.