PENN Medicine

SPRING 2013

USING MAPS TO SHOW PATTERNS OF GUN VIOLENCE

There's No Getting Away from Biological Clocks

Building Medical Bridges Across Cultures

Penn Psychiatry: Into the Mainstream

"Big Data" Rules at Penn

We now live a world of big data, which is transforming every aspect of medicine from the laboratory bench to the clinic and the classroom. Our scientists are regularly interrogating the genome to better understand how patterns of gene and protein expression reveal new dimensions of physiology. Indeed, our language has evolved to include neologisms such as genomics, proteomics, and metabolomics, among others. Our clinicians have embraced the electronic medical record as part of routine care and communication. Increasingly, we mine this vast database to identify variations in care and provide feedback to improve outcomes. In the end, we hope to better link this clinical data with research. Penn was a pioneer in efforts to record lectures for students. We are now leading efforts via Coursera to produce MOOCS (massive open online courses) that can viewed worldwide. Our faculty and students are developing new telemedicine products in Botswana that allow photos of skin rashes or potential cervical cancer lesions to be transmitted by cell phones from remote areas.

Last fall, I received the recommendations from our faculty-led strategic planning process, "Shaping the Future of Medicine." I was pleased to learn that several of the major recommendations speak directly to keeping pace with the growth and use of big data. Specifically, in this domain of the plan, our faculty recommended: 1) Create an Institute for Biomedical Informatics that incorporates computational biology, bioinformatics, clinical informatics, population health informatics, bio-sample management, and large-scale clinical data warehouses; 2) Create a Center for Personalized Diagnostics that will allow us to increasingly tailor treatments to the needs of individual patients; and 3) Evolve towards a more fully integrated electronic medical record to allow patient information and results to move seamlessly across the health system, thereby enhancing multidisciplinary and complex clinical-care services around the patient. As the document stated, investing in state-of-the-art informatics programs "will enable researchers to make advances by harnessing the vast data available from our integrated enterprise to make more accurate and informed discoveries and decisions."

We've listened carefully to these faculty recommendations. Earlier this year, we launched the new Institute for Biomedical Informatics and the new Center for Personalized Diagnostics, which has now been approved by the College of American Pathologists (CAP) and the Clinical Laboratory Improvement Amendment (CLIA). Below, I explain a bit more about these important new initiatives.

The landmark achievement of the International Human Genome Project was to complete a blueprint of the human genome, thereby accelerating the concept of personalized medicine. What we still lack, however, is a way to compile, organize, and put such "big data" to effective use in treating patients. Four years ago, when the Penn Genome Frontiers Institute (PGFI) and the Franklin Institute held a symposium on personalized medicine, Thomas Curran, Ph.D., professor of pathology and laboratory medicine, associate director of PGFI, and deputy scientific director at the Children's Hospital of Philadelphia, noted that "At the present time, we are better at collecting the information than truly understanding it." Even last summer, CNN posted an account titled "Is personalized medicine a myth?" The high costs involved were cited as one crucial reason for skepticism.

As recently as 2001, according to estimates by the National Human Genome Research Institute, the total cost of obtaining a single human-genome sequence was $95 million. By Spring 2007, the cost had dropped to nearly $10 million. Consistent with Moore's Law, which posits that computing power doubles every two years, costs have been dropping sharply. By January 2011, the estimated cost of a complete genome sequence was $21,000 – and according to a graph produced by the NHGRI, the cost is likely to drop to about $1,000 within a few years. In addition to advances in computational power, novel methods for DNA sequencing are increasing the speed and accuracy of the results. It is easy to imagine a day when newborn testing will include complete sequencing of the genome, with the results deposited in a secure database.

The Challenge Ahead

For now, the challenge remains what to do this with all of this information! At Penn Medicine, the Center for Personalized Diagnostics has begun with a focus on the genetic alterations that occur in cancer. Panels of genes have been developed for "solid tumors" and for hematologic malignancies. The ultimate goal is to tailor treatment protocols on the nature of the genetic defects. Rather than base protocols solely on the organ of cancer origin (i.e., lung cancer) or the histology (i.e., poorly differentiated), it might be possible to identify abnormal pathways (i.e., EGFR, BRAF, CKIT) that guide treatment regimens. This information might also be used to avoid the use of drugs that are ineffective, thereby sparing the patient unnecessary side effects. This new approach to treatment is called by different names – personalized medicine, individualized medicine, and (the term preferred by the National Research Council of the National Academies) precision medicine. By any name, however, it is a clear rejection of the "one size fits all" approach to treating patients.

Another dimension of personalized medicine is a broad effort to maximize drug efficacy and minimize side effects. Stephen Kimmel, M.D.,

professor of medicine and of epidemiology at Penn Medicine, explained the opportunity at a luncheon for the media some years back. An estimated 10 billion doses of medicine are dispensed each year in the United States alone. Only one in three treated patients derives a benefit; one in three does not; one in 10 patients experiences side effects – some serious. One in three derives a real benefit: is this truly the best we in medicine can do for our patients? Last year we established the Center for Pharmacoepidemiology Research and Training, headed by Sean Hennessy, Pharm.D., Ph.D., associate professor of epidemiology and pharmacology. Its members are leaders in the development and use of large administrative and medical record databases for studying drug effects – in a way hardly imagined a few years ago.

Penn Medicine also has remarkable core facilities for research, and they are getting stronger, with state-of-the-art instrumentation. For example, our Next-Generation Sequencing Core has three Illumina hiSeq2000s that provide very thorough ultra-high-throughput sequencing. In any given year, our faculty publish hundreds of high-impact papers using this technology. A few years ago, it would have been hard to imagine a project that could map genome-wide changes in the epigenome during a developmental process or in response to a treatment. Now our faculty do this regularly and quickly share their results with scientists worldwide, as the data is available via open-access journals. These are truly "big data" sets, and we will need to continue expanding our capabilities and technologies to keep pace.

Of course, all of these activities require institutional investment. Part of the magnificent gift we received last year from Joel and William Smilow provides support for enhancing our biomedical informatics team and infrastructure. Their naming gift for the Smilow Center for Translational Research appropriately catalyzes the translation of basic research into clinical application.

The will to discover new treatments has always been there. Now, with these wonderful additions to our armamentarium, our ability to organize and harness the necessary data will help us accelerate progress in medicine. ■

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

The cover illustration uses maps created by the Pennsylvania Horticultural Society.

PENNMEDICINE SPRING 2013 / VOLUME XXIV NUMBER 2

ON THE MAP

By Martha Ledger

Charles C. Branas, Ph.D., had been studying gun violence and its connection to geography and place since coming to Penn in 2000. Can greening a blighted vacant lot make people safer and healthier? Branas is using epidemiology's original tool – the map – to find an answer. One of his allies in this quest: The Pennsylvania Horticultural Society.

SIMPLY BECAUSE

"The needs that call Penn Medicine to action in the community are profound." But as the 2013 edition of *Simply Because* goes on to say, Penn Medicine's physicians, scientists, nurses, staff, students, and partners in the Philadelphia community are working to meet those societal needs.

LIVING BY THE CLOCK: THE SCIENCE OF CHRONOBIOLOGY

By Mark Wolverton

Biological clocks are an integral part of life on Earth, from the simplest one-celled organisms all the way to human beings. One Penn researcher describes chronobiology as "a hardwired, fairly inflexible biology, and yet social and economic systems of modern humans provoke it constantly." Penn has become a hotbed of chronobiological discovery.

BUILDING MEDICAL BRIDGES ACROSS CULTURES

By Mark Gaige

Carl Bartecchi, M.D. '64, a veteran of the Vietnam War, has made it his mission to help provide medical training and supplies for a hospital in Hanoi. Shortly after diplomatic ties between the United States and Vietnam resumed in 1995, Bartecchi and his wife, Kay, began the first of what would generally become twice-a-year visits to the country that continue to this day.

BENJAMIN RUSH AND 200 YEARS OF PENN PSYCHIATRY, Part 2

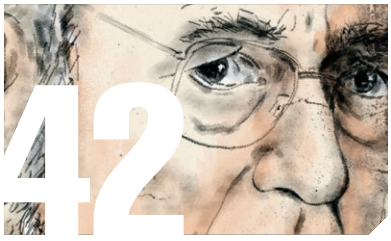
By Marshall A. Ledger

In the years following Benjamin Rush's seminal book *Medical Inquiries and Observations, Upon the Diseases of the Mind* (1812), psychiatry developed slowly. It was in the 1930s when the situation began to improve, at Penn and elsewhere, and psychiatry began to move increasingly into the mainstream. Along the way, Penn faculty members have made many significant contributions to the field.

WHEN ART MEETS SCIENCE

By Karen Kreeger

Lili Guo, a Ph.D. candidate who studies cell death and neurodegenerative diseases, often turns to art to balance her life. Her particular combination of skills and interests has led to her designing more than 15 submitted covers for scientific journals.



C. EVERETT KOOP: A SURGEON, AN EDUCATOR, AND A MAN WHO SPOKE HIS MIND

Widely considered the most influential surgeon general in American history, Dr. Koop had a long and successful career in Philadelphia before entering the national spotlight. He was a vital figure at Penn's School of Medicine and the Children's Hospital of Philadelphia. In one of his returns to Penn, he discussed threats to the doctor-patient relationship.

Departments

Inside Front Cover — THE FIRST WORD
"Big Data" Rules at Penn

2 — VITAL SIGNS
Personalized Diagnostics
Ranking the Schools
Transitions

38 — DEVELOPMENT MATTERS
Thanks a Billion – and Then Some!

45 — ALUMNI NEWS
Progress Notes and Obituaries

Inside Back Cover — EDITOR'S NOTE
A Different Kind of Personalized Medicine

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A New Weapon Against Cancer: Personalized Diagnostics

Many of cancer's genetic underpinnings remain hidden, even from CT scans and MRIs. Penn Medicine's new Center for Personalized Diagnostics, a joint initiative of the Department of Pathology and Laboratory Medicine and the Abramson Cancer Center, is probing more deeply into each patient's tumor with next-generation DNA sequencing. These specialized tests, which can refine patient diagnoses with greater precision than standard imaging tests and blood work, are expected to broaden treatment options and improve their efficacy.

"A tumor's genomic profile is the most critical piece of information for an oncologist to have when they're deciding what therapy to recommend," says David B. Roth, M.D., Ph.D., chairman of Pathology and Laboratory Medicine. The results of tests in the new center "reveal a genetic blueprint of each patient's tumor that is as discrete and singular as a fingerprint."

The center brings together experts in genomic analysis, bioinformatics, and cancer genetics with oncologists who treat patients and design clinical trials to test new therapies.

The first group of patients who are undergoing testing through the center includes those with blood cancers and solid tumors of the brain and lung, as well as melanoma. Throughout 2013, the tests will be expanded for a wider range of cancer patients. Results are available within two weeks – twice as fast as most commercially available testing panels. All new and relapsed patients of the Abramson Cancer Center will receive this testing – conducted via simple blood tests and/or biopsy of tumor tissue or bone marrow – as part of their evaluation and diagnostic process. Physicians and genetic counselors will interpret the results one-on-one to patients and their caregivers. In contrast to the new center's offerings, individual genetic tests are time consuming and expensive to conduct, and they often yield information that is not clinically usable. Since the center began operating earlier this year, however, tests in 80 percent of patients revealed genetic mutations that may be used to alter their course of treatment or clarify their prognosis.

The results of each patient's test will add to an enormous repository of genomic mutation profiles that, combined with the ability to follow patients over time, will help clinical researchers identify new markers and mutation profiles to better predict the course of an individual patient's treatment response and suggest new targets for therapy. As new mutations are detected and novel treatment options are identified, the gene testing panels will be modified and expanded, creating an option for profiling evolving mutations in real time.

– Holly Auer

After Asbestos Exposure, What Next?

Just north of Philadelphia, the communities of West and South Ambler are working to recover from the ramifications of their town's long-closed asbestos factory. Today, residents in these communities remain at risk of environmental exposure and may have an increased risk of developing mesothelioma, a rare cancer caused almost exclusively by exposure to asbestos. To help residents to shape the future of their communities and to explain the potential consequences associated with asbestos exposure, researchers at the Center of Excellence in Environmental Toxicology have been awarded a $1.2 million grant to develop an educational program that uses the communities' history of manufacturing asbestos products and the resulting exposure to asbestos. Funding for the program is provided by the Science Education Partnership Award, which is administered by the National Institutes of Health.

From the late 1880s through the present day, residents of West and South Ambler have had either occupational or environmental exposure to asbestos. As a result, both current and former residents now face potentially serious long-term health consequences. In fact, the Pennsylvania Department of Health has determined that there has been an increase in the rate of mesothelioma in the area compared to Pennsylvania as a whole.

Frances K. Barg, Ph.D., associate professor of family medicine and community health, is principal investigator for the project. Barg, Edward Emmett, M.D., M.S., professor of occupational and environmental medicine, and their team will develop a storehouse of information online and at the Chemical Heritage Foundation in Philadelphia about asbestos-related health risks, will profile people who were affected by living or working near the asbestos materials, and will provide an opportunity for community members and scientists to learn about each other's experiences.

Major components of the project include documenting the history of lower-income African-American and Italian immigrant asbestos workers, their families, and their neighbors in West and South Ambler through recorded interviews; and developing an accessible repository of documents, photographs, news accounts, and scientific data. Educational components of the program will work to inform citizens, scientists, and policy-makers on long-term health effects and other potential consequences from living and working near aging and hazardous industrial sites.

– Katie Delach

Ranking the Schools

For the sixteenth consecutive year, the Perelman School of Medicine has been ranked among the top five research-oriented medical schools in the nation by *U.S. News & World Report*. This year it was

Photograph by Rob Press

Match Madness

In addition to the N.C.A.A. basketball tournament, March is also the month for Match Day, eagerly awaited by thousands of medical students across the nation. It is the culmination of a process that began in the fall through the National Residency Matching Program, which pairs graduating medical students with the hospitals or medical centers of their choice.

At the Perelman School of Medicine this year, 161 students gathered in Stemmler Hall for the emotional ceremony. Seventy-seven women and 84 men received their "residency placement" envelopes, which informed them where they would be spending the next few years of their training.

also ranked #13 among schools with a focus on primary care.

According to the survey results, the medical schools earning a top-5 ranking for research, in order, are: Harvard University, Stanford University, and Johns Hopkins University, followed by the University of California at San Francisco and Perelman tied at #4. The complete survey results as well as the methodology used can be found at USNews.com.

The Perelman School of Medicine also ranked among the nation's top medical schools in five areas of specialty training: Pediatrics (#1), Women's Health (#3), Internal Medicine (#4), Drug/Alcohol Abuse (#5), and AIDS (#7).

According to J. Larry Jameson, M.D., Ph.D., executive vice president of the University of Pennsylvania for the Health System and dean of the medical school, "While it is always prudent not to place too much emphasis on these types of rankings, our School of Medicine's standing in the rankings by *U.S. News & World Report* is a very public recognition of the commitment to excellence by our faculty, students, and staff. We are fortunate to have so many truly exceptional people working together to ensure that we provide outstanding educational programs, pursue pioneering biomedical research, and deliver compassionate care at the highest levels of excellence."

Calling All Informaticians

Penn Medicine has established the Institute for Biomedical Informatics, with support from the naming gift of the Smilow Center for Translational Research. Its mission is to bring together members of the Penn faculty who work in biomedical informatics. According to J. Larry Jameson, M.D., Ph.D., executive vice president of the University of Pennsylvania for the Health System and dean of the Perelman School of Medicine, "We will expand the number of faculty even more to create a wide-ranging program of research and education to find and clinically apply the treatments of the future and to train the next generation of physician-scientists."

John Hogenesch, Ph.D., professor of pharmacology, has been named interim director of the institute. Three associate directors have also been named: John Holmes, Ph.D., associate professor of medical informatics in epidemiology; Klaus Kaestner, Ph.D., professor of genetics; and Curtis Langlotz, M.D., Ph.D., professor of radiology. A national search will be launched for the institute's permanent leader.

Big data is increasingly driving both biological research and clinical care. In biomedicine, this information runs the gamut from bioinformatics at the genome and molecular level, to health-care informatics at the clinical level, to public-health informatics at the population level.

In partnership with the Penn's schools of Engineering and Applied Sciences, Arts and Sciences, Nursing, and Veterinary Medicine, as well as The Children's Hospital of Philadelphia, the institute will tackle challenges directly relevant to patient care, as well as improve basic research that leads to more personalized care. It will also focus on educating the next generation of biomedical informaticians by folding in a new master's degree in biomedical informatics with the existing Ph.D. program in genomics and computational biology and by creating additional graduate and medical training programs as this field evolves.

– Karen Kreeger

Transitions

Joseph W. St. Geme III, M.D., has been named chair of the Department of Pediatrics, effective July 1, 2013. He succeeds Alan R. Cohen, M.D., a long-time member of the Penn faculty who has served as chair since 2001. St. Geme will also become physician-in-chief at The Children's Hospital of Philadelphia. Currently the James B. Duke Professor of Pediatrics and chair of the Department of Pediatrics at Duke University Medical Center, St. Geme has focused his research on host-pathogen interactions that involve pathogenic bacteria. His work has relevance to developing a vaccine that would be broadly effective against *Haemophilus influenzae*, a common cause of local respiratory tract disease and serious invasive infection. Among his clinical interests are pediatric infectious diseases, infections of the respiratory tract and central nervous system; tick-borne infections; and microbial pathogenesis.

St. Geme took his pediatric internship and residency at CHOP and was chief resident in pediatrics 1987-88. An alumnus of Harvard Medical School, he was a postdoctoral fellow at Stanford University, first in microbiology and immunology and then in pediatrics. In 1992, he was appointed assistant professor of

pediatrics and molecular microbiology at Washington University in St. Louis. In 2005, he joined Duke University in his

Letters

More About Lymphedema

In response to Martha Ledger's article "Wiser Scientist" (Fall 2012) and Dr. Schmitz's recounting of a lymphedema patient's lament that "the best I can hope for, if I do everything right, is that it [lymphedema] doesn't get any worse" – I submit that there is a good chance that a patient's lymphedema can be quite successfully treated, as long as oncologists make prompt referrals to certified lymphedema specialists for comprehensive decongestive therapy. Penn Therapy and Fitness has such a program at 36th and Market, at Penn Medicine at Rittenhouse, and in Radnor.

With regards to the notion that there are "biochemical agents" or "biomarkers" associated with obesity that may increase the incidence of a primary tumor or a tumor recurrence, I submit that toxins from the food supply bioaccumulate in the adipose tissue sink and may act as xenobiotics or endocrine disruptors, potentially leading to carcinogenesis. Vitamin D (a hormone) deficiency or insufficiency is correlated with increased cancer incidence – could it be that xenobiotic toxin-induced endocrine disruption is etiologic? Perhaps protective immunity is down-regulated and epigenetic phenomena unmask oncogenetic expression. Perhaps it is not the excess adipose tissue that increases cancer incidence, but rather what is contained at much higher body loads within the excess adipose that is responsible. In addition, the average diet contains an overabundance of pro-inflammatory molecules (markedly excessive sugar, animal fat [bioaccumulated toxins?], and fried, blackened, and barbecued foods) – this inflammation has been implicated as a cofactor in carcinogenesis.

I hope future research funding is directed toward more definitively answering the questions that I have posed. I wish Dr. Schmitz the best in her research endeavors.

L. Matthew Schwartz, M.D., G.M.E. '89
Clinical Assistant Professor, Department of Physical Medicine and Rehabilitation

Kathryn Schmitz, Ph.D., M.P.H., responds:

How wonderful to discover a clinical colleague interested in lymphedema through this forum. I look forward to reaching out to Dr. Schwartz after this letter exchange. As to the comments about the lymphedema patient's lament and Dr. Schwartz's reply, I could not agree more that lymphedema can be successfully treated and that Good Shepherd Penn Partners (formerly known as Penn Therapy and Fitness) offers world-class lymphedema care. Further, I could not agree more with the qualifier offered by Dr. Schwartz: "as long as oncologists make prompt referrals. . . ." Within that phrase lies the challenge for a broad variety of clinical issues faced by those who have undergone necessary but toxic cancer therapies. There are multiple barriers to addressing persistent adverse effects of cancer treatment, including but not limited to lymphedema. One barrier is the fractured delivery of health care: surgery, radiation, chemotherapy, and survivorship follow-up may all occur in separate health-care systems. Other barriers are lack of established relationships between the oncology, general surgery, and plastic surgery professions and the rehabilitation and exercise professions, such as exists between the cardiac surgery or orthopaedic surgery and rehabilitation professions (rehabilitation medicine, physical and occupational therapy, and exercise physiologists). Further, there may be a sense by patients and their health-care providers that these cancer treatment sequelae are "expected" and normal and that they simply need to be tolerated.

current positions. During St. Geme's tenure as chair, Duke's Department of Pediatrics established four new divisions and created several new multidisciplinary clinical programs, including pediatric obesity, autism spectrum disorders, and neuromuscular disease.

Among St. Geme's many honors, he was elected to the Alpha Omega Alpha Honor Medical Society while a resident at Penn. In 2010, he was elected to the Institute of Medicine of the National Academy of Sciences. St. Geme has also won several teaching honors, beginning with the award for Outstanding Resident Teacher at Children's Hospital of Philadelphia.

St. Geme has been consistently supported by grants from the National Institutes of Health. He is an editor of the *Nelson Textbook of Pediatrics*, 19th Edition, published in 2011, and was named associate editor of the *Journal of Clinical Investigation* last year.

Dahlia M. Sataloff, M.D., was named chair of the Department of Surgery at Pennsylvania Hospital. She succeeds Robert D. Fry, M.D., who had led the department since 2006. Sataloff has been a member of the PAH surgical staff since 1985. In 2005, she was named director of the Integrated Breast Center and vice chair of the department. Sataloff has been consistently recognized in *Philadelphia* Magazine's "Top Docs" for the treatment of breast disease and in Castle Connolly's *America's Top Doctors for Cancer*. She is a Fellow of the American College of Surgeons.

H. Lee Sweeney, Ph.D., was appointed inaugural director of the Center for Orphan Disease Research and Therapy. Sweeney, the William Maul Measey Professor, has served as chairman of the Department of Physiology since 1999. As a basic scientist whose research program has included a substantial focus on inherited diseases, he has been a passionate advocate for research funding and has worked extensively with patients and advocacy groups. Since 2000, he has been scientific director of Parent Project Muscular Dystrophy, whose mission is to fund research and advocate for Duchenne muscular dystrophy care.

According to the memo announcing the appointment, "Sweeney's combination of expertise, experience, and enthusiasm makes him an ideal leader for our new interdisciplinary center."

Sweeney's basic research is focused on the molecular motors of the myosin proteins that are responsible for generating contractile forces in muscle. In the popular press, Sweeney is well known for his gene-therapy approaches to permanently block the age-related loss of muscle size and strength in mice. The technique suggests that therapies for humans could reverse the feebleness associated with old age or slow the muscle-wasting effects of muscular dystrophies. He has also been involved in developing small-molecule therapy for muscle disease, a drug (called

PTC124) that would suppress nonsense mutations in a variety of genetic disease models.

Sweeney is a Fellow of the American Heart Association and a recipient of the Perelman School's Stanley N. Cohen Biomedical Research Award. ●

The number of survivors seen in oncology clinics is growing and is expected to strain available and expected resources in the near future. Survivorship care research and clinical endeavors are under way at Penn, under the direction of Drs. Jun Mao (Family Medicine physician, director of Integrative Oncology), Linda Jacobs (Oncology nurse practitioner, director of the LiveSTRONG Survivorship Center of Excellence), James Metz (Radiation Oncologist, editor in chief for Oncolink), Carrie Stricker (Oncology nurse practitioner, researcher), and Mously Le Blanc (director of Cancer Rehabilitation, Rehabilitation Medicine Physician), among others. In particular, the Breast Translational Center of Excellence (led by Angela DeMichele, M.D., M.S.C.E., and Lewis Chodosh, M.D., Ph.D.) is working to ensure the qualifier "as long as oncologists make prompt referrals" becomes the default for all patients.

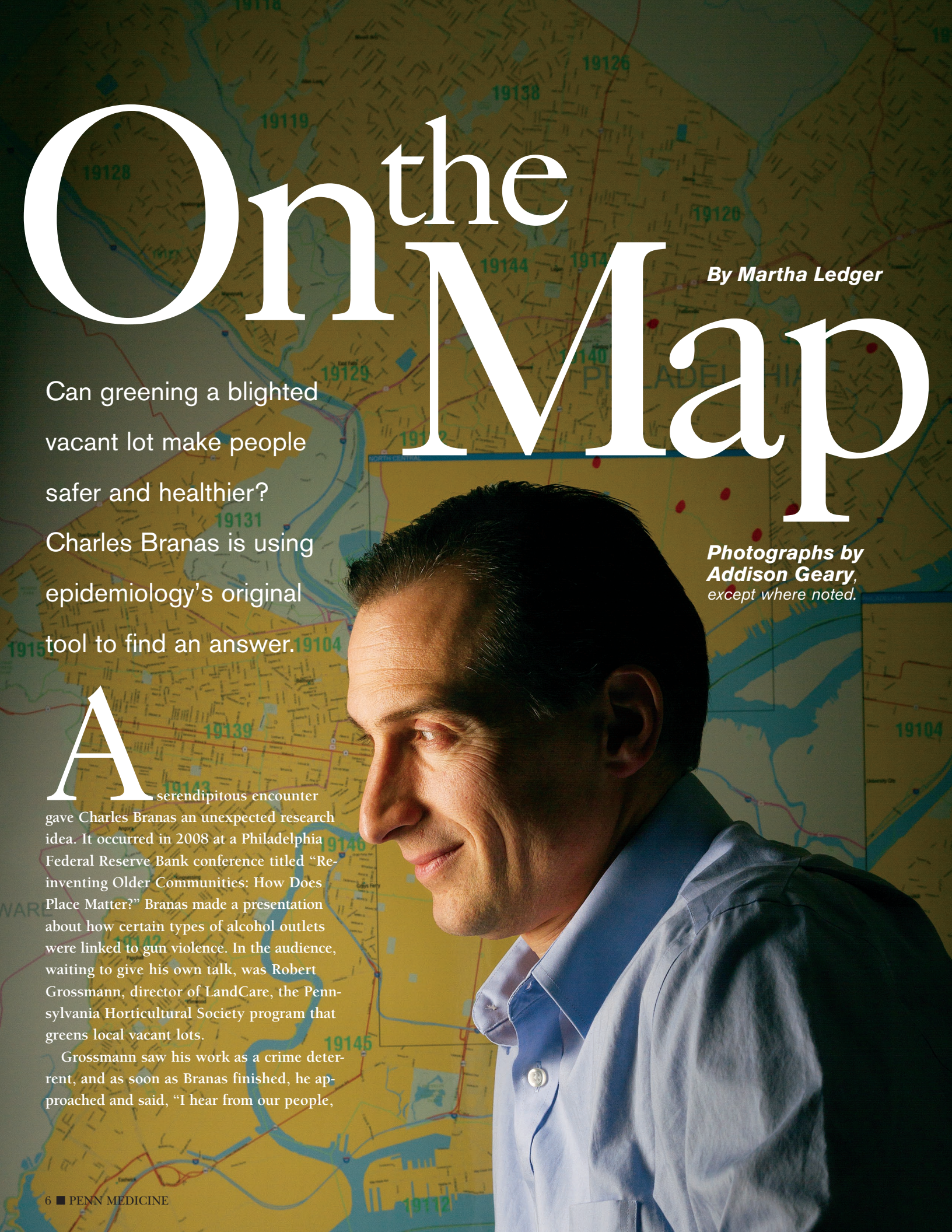
With voices like Dr. Schwartz's in the mix, it is certain that referrals to physical therapy and rehabilitation medicine will be among those prompt referrals.

Dr. Schmitz is associate professor of epidemiology.

On the Map

By Martha Ledger

Can greening a blighted vacant lot make people safer and healthier? Charles Branas is using epidemiology's original tool to find an answer.



Photographs by ***Addison Geary****, except where noted.*

A serendipitous encounter gave Charles Branas an unexpected research idea. It occurred in 2008 at a Philadelphia Federal Reserve Bank conference titled "Re-inventing Older Communities: How Does Place Matter?" Branas made a presentation about how certain types of alcohol outlets were linked to gun violence. In the audience, waiting to give his own talk, was Robert Grossmann, director of LandCare, the Pennsylvania Horticultural Society program that greens local vacant lots.

Grossmann saw his work as a crime deterrent, and as soon as Branas finished, he approached and said, "I hear from our people,

just anecdotally, that when we green these lots, crime goes down." Branas wanted to know more.

Charles C. Branas, Ph.D., professor of epidemiology and director of the Penn Cartographic Modeling Lab, had been studying gun violence and its connection to geography and place since coming to Penn in 2000. "I had been describing various threats to health and safety for years," he says, "and I really wanted to turn the corner and start doing something to *improve* health and safety." The conversation between the two set him moving in what would be a challenging but important new direction.

Branas's "describing" years were powerful ones. He was principal investigator of numerous studies related to gun violence. In 2004, he and his colleagues published a nationwide study of geographic variations in firearm death that went on to be cited in landmark Supreme Court decisions on the topic. The study analyzed more than one-half million firearm deaths occurring in the 1990s for every county in the U.S. It found the risk of death by firearms equal in rural and urban areas: homicide more common in cities – not a surprise – and suicides alarmingly prevalent in the countryside, where they were largely overlooked.

Branas also received one of the three major gun-violence research grants the National Institutes of Health (NIH) has awarded over the last 40 years. It funded his study on the relationship between alcohol availability and gun violence – the work he presented at the Federal Reserve Bank conference. Analyzing 677 gun assaults that occurred in Philadelphia between 2003 and 2006 (plus 684 controls randomly sampled from the city's adult population), he showed that heavy drinking where take-out alcohol venues were plentiful significantly increased the risk of being shot. Heavy drinking in bars and taverns, even in neighborhoods rife with gun violence, turned out to be less of a risk.

Published in the journal *Alcoholism: Clinical and Experimental Research* in 2009, the findings gave big cities a way to reduce gun violence without getting embroiled in gun-rights issues. They could modify environmental factors related to alcohol: for example, limit the hours take-out alcohol can be sold, prohibit sales to visibly intoxicated customers, crack down on public drunkenness, or selectively shut down nuisance outlets.

Branas had also already hit upon the relationship between vacant properties and violence. Not long before the conference, a student of his at the time, J. Nadine Gracia, M.D., M.S.C.E. '08 (who went on to be a White House Fellow and is now the Deputy Assistant Secretary for Minority Health), had mapped violent crime in Philadelphia, plus a host of other factors, such as vacant properties, poverty, unemployment, race, ethnicity, and education.

"The map of vacant properties was almost identical to the map of violent crimes, more so than the maps we made of a dozen other well-known indicators of disadvantage," says Branas, the senior author of the study. "The match was more than just by chance."

Gracia and Branas showed that every new vacancy in the study area corresponded to an 18.5 percent increase in violent crime and an even greater increase – 22.4 percent – in violent crimes committed with guns, but the study had limitations. The records they used had identified vacant properties overall, but didn't differentiate between abandoned buildings and empty lots. The researchers couldn't determine which, if either, was more responsible for gun crimes. Moreover, they couldn't say which had come first: Had the presence of vacant properties invited crime, or had crime emptied neighborhoods, driving residents and businesses elsewhere?

Grossmann's experience resonated with their findings. He could speak to blighted lots as hot spots for crime, describe open-air drug markets – "with tables and awnings" – set up amid the weeds and debris, report on guns discovered there by his contractors and bodies found by the police. Grossmann recalled how residents had once fought the demolition of a condemned house because they feared an empty lot more. He knew that people often walked down the center of the street, giving wide berth to lots that were wildly overgrown.

After the greenings, Grossman noted the disappearance of some notorious open-air markets. Residents also reported less drug activity in their neighborhoods. Neighborhood retailers corroborated these views when they com-

How it looked before and after greening, near the intersection of Cecil B. Moore Avenue and N. 4th Street.

plained that the dealers weren't around to shop in their stores anymore.

Even more useful to Branas than the wealth of anecdotal information were the meticulous records Grossmann had kept on 4,436 lots greened between 1999 and 2008. The data were available to researchers and in the form of GIS (geographic information systems) maps. Branas invited Grossmann to attend a small internal meeting at Penn where broad-based research on vacant space was being presented.

"He's really open to exploring things," Grossmann says of Branas. "From the start, he was totally engaged, trying to understand every aspect of our work, seeing how it related to his own. There's always been a good give-and-take between the practical groundwork that we do and his academic expertise."

Starting with Grossmann's maps, Branas designed a study to measure the effect of greening on health and safety. A control group was drawn from the almost 55,000 untreated lots Philadelphia was estimated to have at the time. "It was a 'found' or quasi-experiment," Branas says, "something epidemiologists are always on the lookout for."

The Cartographic Modeling Lab then gathered data from the Philadelphia Police Department on the exact location and nature of crimes, as well as health information from the Philadelphia Health Management Corporation, which biannually surveys Philadelphia residents about their health. "Our researchers incorporated everything into a larger mapping system," Branas explains, "allowing us to analyze, to make maps, to make visual what had happened in and around those vacant lots before and after they were greened."

"All this," he adds, "is part of what the CML and cartography are able to do. Without it, we wouldn't have been able to do our analysis." (For the roots of epidemiological mapping, see box on p. 11.)

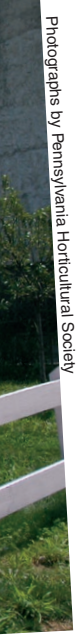
The analysis, published in the *American Journal of Epidemiology* in 2011, showed a significant reduction in violent crime – particularly gun crimes – around lots that had been greened. Gun-related crimes were down between 7 and 8 percent, and Branas was able to confirm that they didn't just shift to nearby streets. (He also reported reductions in vandalism, criminal mischief, and stress, plus increases in how much people exercised.)

Branas has two hypotheses for the reduction in gun-related crime. One is the widely cited "broken windows" theory proposed by political scientist James Q. Wilson, Ph.D., and criminologist George Kelling, Ph.D., in 1982. It claims that broken windows, graffiti, trash-strewn streets, and all other visual aspects of blight actually promote crime.

The opposite happens when greening replaces blight: people feel more invested in the area. They keep it clean. If anything disorderly occurs, they call the police. Criminals are less at home in the space.

While Branas accepts this explanation – for him, "broken windows" is not just a theory anymore – his work is some of the first to challenge this theory in the real world and make it more than just academic. He notes, for example, that it's really difficult to hide an illegal gun in or around a cleaned and greened lot and believes there is a physical component to reducing gun violence.

Branas's results received a lot of press coverage, and people who knew his work saw it as an extension of his gun research. "But quite frankly," he says, "we looked at more than 20 outcomes that potentially related to health and safety." As he points out, only two, which he had casually added into the mix, "were about guns. It just so happens that one of those gun-oriented outcomes carried the day."



Photographs by Pennsylvania Horticultural Society

Branas has designed a vastly more ambitious study that combines greening, health, and crime. In the process, he's addressing limitations of the found experiment, one example being a possible "selection bias." He explains: Maybe greening occurred somewhere because constituents complained to their councilwoman about a particular lot, and the councilwoman then called the Pennsylvania Horticultural Society. The fact that someone has the wherewithal to complain might mean that a neighborhood is already improving. It may be that, in such a case, Branas wasn't measuring the impact of the greened lot but rather the social connectivity of the neighborhood. "The best way to handle this sort of thing," he says, "is to randomly assign the lots for treatment, just like you would, say, in a clinical trial of a drug."

This is precisely what he is now doing, through a five-year community trial funded by the NIH. Today, Philadelphia has an estimated 40,000 vacant lots, more than a quarter owned or controlled by the city because of complaints lodged against them. Hundreds have been randomly selected for the trial. A third will remain as they are. Another third will get monthly trash cleanups, but nothing more. A final third will get LandCare's standard treatment: They will be cleaned, enriched with topsoil, graded, planted with grass and trees, enclosed with simple wooden fencing, and maintained monthly.

The cooperation of several municipal agencies has made this study possible. "Only an amazing communicator – which Branas is – could have gotten everyone's buy-in," says Brian Strom, M.D., M.P.H., the George S. Pepper Professor of Public Health and Preventive Medicine and former chairman of Branas's department.

The city has much to gain from this study. It is already financing LandCare's greening work. If the program is shown to enhance health and reduce violence, Philadelphia can redouble its efforts in what is a very inexpensive intervention. Moreover, the simplicity of the greening treatment means it can easily be extended to lots outside the study, as well as to other cities across the United States.

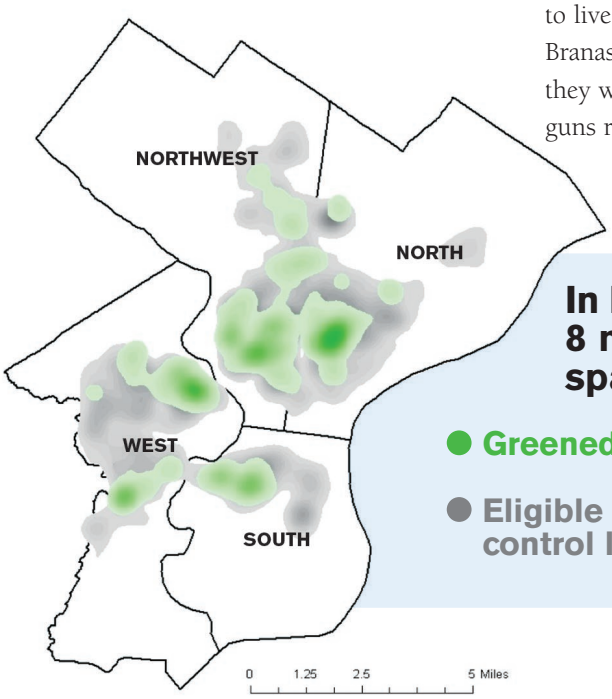
Branas will now be looking at more than 100 trial outcomes related to both health and safety, with a special focus on substance abuse. His research team will be taking physical measurements, such as blood pressure and weight, and also asking neighborhood residents about intangibles such as stress, happiness, and trust. Last year, Eugenia Garvin, M.D., then a Robert Wood Johnson Clinical Scholar who earned a master's degree in health policy at Penn last year, led a pilot study proving that this kind of place-based community trial is doable. (Branas was senior author of the study.)

Philadelphians from the local neighborhoods, with experience doing door-to-door interviewing, have been hired and trained to administer the survey. In addition to a great group of local interviewers who can really connect with people, "there's also a lot of good will in the neighborhoods," Branas says. "When people hear that we're doing a survey about health and the environment, with the hope of improving both, many say, 'That's really important to me. I want to take this survey if you think it's going to help.'"

Branas is covering yet another base, this one also with boots on the ground. "Epidemiologists function in the stratosphere of numbers," he says. "We'll find some statistical relationship that *we* think is really important, but it's an uphill battle to explain it, bring it back down to earth." For what's called "biological plausibility" – an important criterion in explaining cause-and-effect – he works with anthropologists and ethnographers who observe the actual goings-on in a study area.

In this project, Branas is collaborating with Philippe Bourgois, Ph.D., a Penn Integrates Knowledge professor and the Richard Perry University Professor, with appointments in the Department of Anthropology (School of Arts and Sciences) and the Department of Family Medicine and Community Health (Perelman School of Medicine). Bourgois is well known for ethnographic research on homeless drug abusers. More generally, he studies the beliefs and social practices of highly vulnerable populations, so that public health policy can help them effectively.

Some of Bourgois's students have gone to live in neighborhoods that figure in Branas's study. Among many other things, they will try to answer the question "Are guns routinely hidden in blighted lots?"



In Philadelphia, 8 million ft² greened space from 1999-2008

- Greened vacant lots (n = 4,436)
- Eligible but ungreened control lots (n = 13,308)

Staff members of the Penn Cartographic Modeling Lab include, from the left, Krista Heinlein, Karl Dailey, Tara Jackson, and Vicky Tam.

Residents say they are, as do LandCare's contractors and the police. But Branas needs scientifically based observations and detailed descriptions of how they are stashed and used – how these and other effects of the greening actually work to change health and safety.

During his academic training, Branas deliberately linked health and environment. Following an undergraduate major in mathematics – "he is phenomenally quantitatively oriented," says Strom – he studied at Hahnemann University (M.S., 1993), focusing on emergency medical services. His Hahnemann years were among Philadelphia's most violent, when homicides numbered more than 500 in one year, a city record. Branas saw the dead and wounded in the emergency room, on ambulances, and in the morgue.

Even back then, Branas thought of gun violence as a public health problem. "When you're shot," he points out, "you end up in a clinic, the hospital, or the morgue – all parts of the public health system. So it's obvious that public health has a role to play in preventing these deaths."

When he went on to Johns Hopkins University (Ph.D. in health policy, 1997), he also trained in the School of Public Health and in the School of Engineering's Department of Geography and Environmental Engineering. The latter offered "location science" – a specialty that analytically determines the most advantageous places to site businesses, stadiums, medical services, and more. The late Charles ReVelle, Ph.D., who pioneered the specialty, was a mentor of his, and Branas acquired the tools to study and improve delivery systems for emergency medical services, a field in which he still does half of his research. A sense of place and physical environment, spatial visualizations, geographic intelligence, and mapping all became part of his repertoire.

A relationship between health and environment is also inherent in public health and epidemiology, and both disciplines present health problems in terms of the same framework: host, agent and related vector, and environment.

A classic example of the model is a population (host) being infected with malaria (agent) by mosquitoes (vector) in a swampy area (environment). Interventions to prevent or mitigate the disease can be aimed at any of the components. For example: Teach people how to use bed nets; develop drugs to treat malaria; re-engineer the mosquitoes, which the Gates Foundation is now doing; drain the swamp where the mosquitoes are breeding. Were Branas tackling this public health problem, he'd seriously explore environmental change – e.g., filling in the swamp. "It's a simple intervention that could produce lasting effects," he says, "even after funding and treatment programs have left."

Change the malaria model to a gun-violence one: People are injured or killed by guns in blighted urban neighborhoods. Branas's study of greening vacant lots measures the effect of an environmental change, the replacement of blight with grass, trees, and fencing. "People have spent decades focusing on the firearm [agent]," he points out, "and it has only gotten us so far. Environmental change, on the other hand, can affect illegal firearm use, which, in turn, reduces negative outcomes such as violence.

"I'm not advocating we forget about other parts of the model," Branas continues, "but we've focused much less on aspects of the environment, and I think big improvements in health can be had [through it]."

Strom has come to appreciate Branas's approach: "Charlie has educated me, and I'm convinced," he says. "[Environmental] solutions are actually good ways of solving many problems. They're practical, easy to implement, and inherently effective. For example, you can tell people not to drive fast, but it doesn't slow them down. You put in speed bumps, and it fixes things in a way that works."

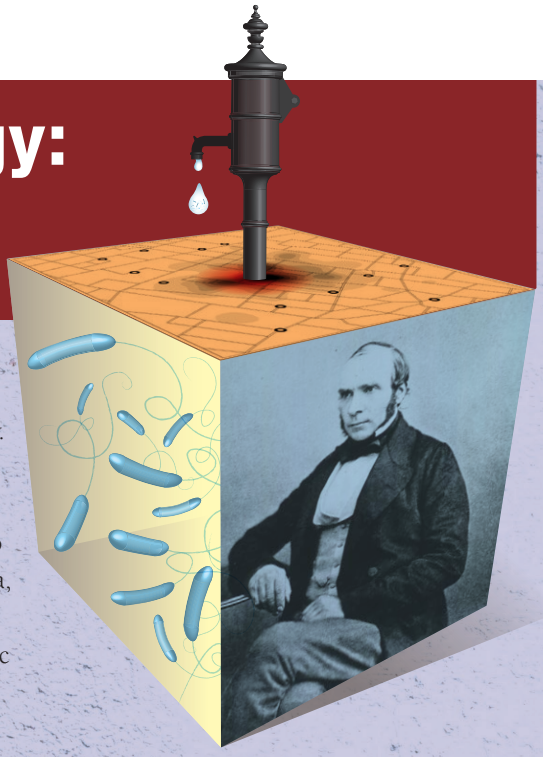
Branas is also thinking beyond small and discrete problems. He mentions a 2003 Institute of Medicine report that

suggests the health of a significant segment of the population won't be improved without correcting the context in which this population lives. As he puts it, "The things that surround us every day – whether it be noise, unhealthy air, lack of a social network, or blight – all have meaning to our health."

When presenting his work, as he did in February at a program given by the Penn Institute for Urban Research, Branas describes three criteria he thinks will make current public health projects more effective. They should involve structural change that affects the basic contexts in which people live. They should be scalable so that they improve the health of large numbers of people. And they should be sustainable so that they survive after the funding that set them up ends.

Greening vacant lots is one example. Branas also points to some newly designed public housing in Seattle that incorporates air-quality features to reduce asthma, which is the most prevalent serious, chronic childhood illness across the nation. He also mentions Charlotte, N.C., where a reduction in obesity and body mass index followed the inauguration of a newly built light rail system, as people

Epidemiology: Looking Back to Move Ahead



Charles Branas's current research on the effects of greening vacant lots has roots in the very origins of epidemiology.

The place was London, England, the year 1854, and while summer was turning into fall, cholera devastated the Soho section of the city. Thousands fled the area, and 616 people died. Everyone, including educated people, blamed the epidemic on bad air.

Physician John Snow wasn't satisfied with this explanation, and, searching for something better, he made a map showing where each sickened person lived. The cases clustered around the public water pump at Broad and Little Windmill streets, and he hypothesized that contaminated water was causing the deadly illness.

The outbreak was already subsiding when he did his mapping. But it ended definitively when, at his request, city officials removed the pump's handle, making the water inaccessible. For his investigative method and finding, Snow is hailed as the father of modern epidemiology.

Snow, his map, and the pump handle have great meaning for Branas, who has always studied health in terms of place. Like Snow, he sees changes in the physical environment as the solution to various problems. His work, like Snow's, encompasses populations rather than individuals. And as Snow did with cholera, he analyzes health phenomena through mapping.

"Today's tools are more sophisticated, but the basic insights are the same," Branas says. "A map is nothing more than a complex collection of information on a single sheet of paper. Good maps quickly show the relationships and tell stories that are otherwise difficult to see."

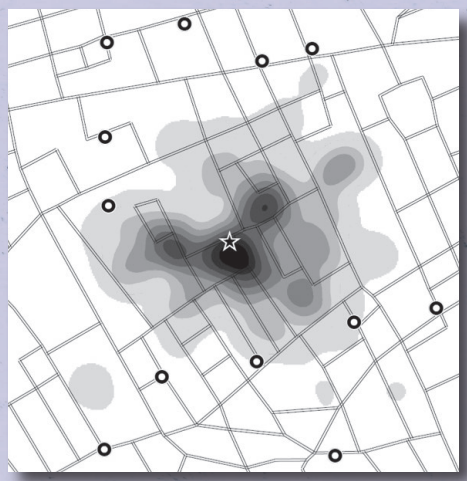
Branas and the University's Cartographic Modeling Lab, which he directs, undertook a re-rendering of Snow's map. "There was a high-profile redo in 1956," Branas says with a smile, "but we knew we could do better." The new map is an overlay of amorphous shapes that increase in tonal value from pale grey at the periphery to solid black at the center, where a star marks the pump. "With Snow's original map, you need a lot of explanation to figure out what's going on," he says. "With ours, the star is in the middle of the darkest blot, and you immediately know that's the pump that needs to have the handle removed."

Different Eras of Epidemiology

At first glance, Branas's attachment to epidemiology's founder might seem predictable. Actually, it's not. Epidemiology since Snow's time has undergone several major shifts to which scholars have retrospectively attached names. Snow is part of the Sanitary Era, which extended into the 1920s and included environmental public health improvements, such as the chlorination of water and better sewage systems.

Advances in microbiology ushered in the Infectious Disease Era, during which epidemiologists tracked the effects of antibiotics and vaccines on transmitted diseases. That era faded when scientists believed – wrongly – that they had successfully conquered the most troublesome microorganisms.

It was supplanted, mid-century, by the Chronic Disease Era, which still holds



sway. A majority of today's epidemiologists study an individual's risk – due to behavior or life-style or genetics – of getting a disease such as cancer, diabetes, or COPD.

Starting in the mid-1990s, some in the field began to advocate for a broader approach that would balance risk-factor studies with other public health concerns, especially health issues arising from social and contextual problems. Epidemiologists Mervyn W. Susser and Ezra S. Susser, writing in 1996, advised, "To look forward, we do well to look backward for guidance." The change they sought is well under way, and Branas is part of it.

– Martha Ledger

gave up driving to work and walked more to and from stations.

The outcomes are not always obvious from the interventions, Branas notes. "It's very challenging to put the pieces together and come up with something successful. But it's important to try and, wherever possible, scientifically document what happens."

The word *greening* somewhat underdescribes what happens to the blighted lots. They are turned into little parks, with a fence that defines their perimeters. The fence is not intended to keep people out: it is just two horizontal rails, knee- and waist-high, always with an entry large enough for a lawn mower. After the greening, the lots are cleaned and the grass is mowed on a regular schedule. A passerby can view the site in its entirety; there are no hiding places for guns or bodies. The fence and the trees planted inside are intended to draw attention to the setting. Drug dealers don't set up out in the open.

Branas hypothesizes that the greened lots may do much more than just lessen crime and gun use in a neighborhood. Those results are clearly beneficial; they represent the removal of a health threat. But Branas's hunch is that the greened lots are actually promoting health, and in a profound way.

When a neighborhood is deteriorating and plagued by crime, he explains, people retreat into their own spaces. They put up barriers so they can't be seen and can't see out. They cease to take part in life on the street. While no one observes it, conditions there become progressively more disordered, and then people rarely go out at all. They stop talking to their neighbors. They get no exercise. They become isolated, sedentary, stressed, and susceptible to a host of mental and physical issues.

Based on the study Branas already completed, LandCare has stepped up greening projects near schools, recreation centers, and community gardens to support and protect those places where human interaction already exists. Branas's theory is that greened lots on a wider scale can reverse the unhealthy hunkering down of whole communities. They can draw people out onto the street again, to connect with their own geography and, more importantly, with one another. ●

Charles Branas checks out the kind of blighted area that could use a greening.

Simply Because

A glimpse of Penn Medicine's many efforts to serve its surrounding community

"The needs that call Penn Medicine to action in the community are profound. Twenty-five percent of Philadelphians live in poverty – that's nearly 400,000 adults and children – and one in seven city residents has no health insurance. Hunger and homelessness remain, still, throughout the city. These societal problems only make health problems that much harder to address, but doing whatever we can to help is in our nature here."

That rather sobering paragraph introduces the reader to the 2013 edition of *Simply Because*, the community benefit report of the Perelman School of Medicine and the University of Pennsylvania Health System. But as the introduction goes

on to say, Penn Medicine's physicians, scientists, nurses, staff, students, and partners in the Philadelphia community are confronting these challenges, dedicated to serving "those who might otherwise go without."

What follows are snapshots from this year's report.

How many teaspoons of sugar are in one glass of iced tea? Which farmers' markets accept WIC and SNAP vouchers? What's a pancreas?

Answers to these simple questions can empower and motivate people to make lifestyle changes that can greatly improve their health and that of their children. That's the goal of the hundreds of nurses from across Penn Medicine who participate throughout the year in community outreach programs such as HUP's **Nursing Community Outreach Program**. In particular, nurses are focusing their energy and efforts on hypertension and diabetes education.

"People are actually very excited about talking with us, and very honest," says William Hudson, B.S.N., R.N., O.C.N., director of Penn Presbyterian's Magnet Program. "Nurses have always been some of the most trusted professionals. People are really honest with us, because we're with them from birth until the end of life."

Hypertension is called the silent killer, quietly taxing the heart and vascular system for years before patients become sick enough to seek help – often too late, only when they suffer a stroke or heart attack. The condition affects African-American men at a much higher rate than the rest of the U.S. population; more than 40 percent of them have high blood pressure, many without knowing it.

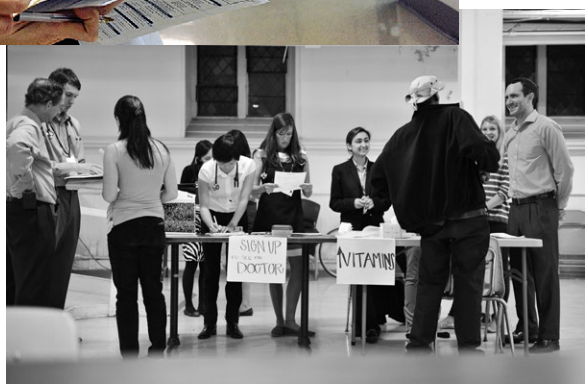
Penn Medicine's **Cut Hypertension** program, which began in 2010, is trimming that risk bit by bit. Twice a month on Saturdays, a corps of Perelman School of

Medicine students heads to a West Philadelphia barber shop, Philly Cuts, to provide a quick blood pressure check to men waiting for a trim. The screenings have revealed that as many as half of the men had hypertension. Though the medical students involved in the program don't treat the men's high blood pressure, they educate them about the seriousness of the condition, encourage them to seek a doctor's care, and help make a match to a local physician.

"The barbers who work in the shop are really important to the program," says Michelle Muyikwa, who is among the leaders of the student group. "When we have people who are scared or reluctant to be screened, we know we have that sort of gentle, friendly encouragement from people they trust in a setting where they're really comfortable."

With five minutes, an ophthalmoscope, and eye drops, Prithvi Sankar, M.D., can prevent blindness. He can quickly check a patient's vision, field of vision, and eye pressure. The ophthalmoscope allows him to evaluate changes to the optic nerve. The eye drops treat glaucoma, a leading cause of blindness.

Sankar, an associate professor of clinical ophthalmology and director of student education for the Department of Ophthalmology at Penn's Scheie Eye Institute, leads the **Penn Sight Savers**, a team of Scheie doctors and medical students. This small band of eye experts holds free screenings at community health fairs throughout West Philadelphia.



Pregnancy, poverty, and a lack of access to health care – especially when compounded by language barriers – make for a dangerous combination. In 2008, to help women facing that exact situation, Jack Ludmir, M.D., professor and chairman of the Department of Obstetrics and Gynecology at Pennsylvania Hospital, created **Latina Community Health Services**. The program operates as part of Puentes de Salud and Pennsylvania Hospital's Women & Children's Health Services, serving Hispanic patients, many of whom are recent immigrants, often undocumented, to the United States.

The circumstances Ludmir's patients grapple with may be dire, but they are no match for the strength of a Latina mama. "Pregnancy gives them the motivation and the power to take charge of their health for the sake of their babies," he says. "They are excellent patients with high compliance rates."

And then they show other women how to do it. Ludmir and members of Puentes, in conjunction with a nurse liaison to the community, recruit former patients to become "promotoras." After receiving basic training, they teach health and wellness to their own communities, spreading knowledge that can help other women have healthy pregnancies and give their babies the best start in life. ●

The full Simply Because is accessible at http://www.uphs.upenn.edu/news/publications/simply_because_2013.pdf

LIVING BY THE CLOCK:

THE SCIENCE OF CHRONOBIOLOGY

By Mark Wolverton

Photographs by Tommy Leonardi, except where noted.

Biological clocks are an integral part of life on Earth, from the simplest one-celled organisms all the way to human beings.

Amita Sehgal, shown here with Christine Dubowy, a graduate student, has found genes that regulate the 24-hour cycle of rest and activity.

The clock never seems to stop. Every day, it seems, we're fighting it: rushing to get to work, getting errands done, catching whatever sleep we can. There's never enough time to do what we need or want to do, and just when we almost seem to get caught up on the weekends or our days off, the clock keeps going and the merry-go-round starts all over again.

That's life for most people in our hectic 21st-century society. Undoubtedly, most of us have occasionally cursed creators of the merciless work schedules, keepers of the deadlines, masters of the timebound obligations by which our economy and society continuously operate. But as arbitrary as they may sometimes seem, clocks, calendars, and schedules aren't an invention of humans. Clocks – mechanisms to track and mark the passage of time – are an integral and indispensable part of life on Earth, from the simplest and most primitive one-celled organisms all the way to human beings.

The study of how biological clocks work to control and regulate almost every function of life is called chronobiology. It's a rich discipline encompassing a broad range of sciences, synthesizing their techniques and viewpoints in new and exciting ways. And almost without even trying to, the University of Pennsylvania has become one of the world's leading centers of chronobiology, with cutting-edge research that involves almost every one of Penn Medicine's science departments and several departments of its hospitals.

"Chronobiology is biological timing," says Amita Sehgal, Ph.D., the John Herr Musser Professor of Neuroscience and a Howard Hughes Medical Institute Investigator. "It basically refers to the process by which organisms time physiology and behavior, so that everything takes place in a rhythmic fashion." The persistent rhythms of life, the body clocks that control when you wake, sleep, eat, digest food, and perform nearly every other function of a living organism, are all the province of chronobiology.

> Chronobiology, says **Amita Sehgal**, "basically refers to the process by which organisms time physiology and behavior, so that everything takes place in a rhythmic fashion."

Although humans have always been at least subliminally aware of how their own bodies and other life forms are affected by natural rhythms such as the day-night cycle, the seasons, and the tides, science paid little attention to such phenomena for most of human history. In the 18th century, curious types such as Swedish naturalist Carl Linnaeus and French astronomer Jean-Jacques d'Ortous de Mairan noted how certain plants responded to different times of day or observed how the behavior of animals varied with light and dark. But no one entertained the idea of an actual biological clock within the body. Perhaps it was because natural rhythms are so all-pervasive and, well, natural, they were simply taken for granted – or it may be that even as Enlightenment science seemed to increasingly reveal the workings of a mechanistic, clockwork universe guided by Newtonian physics, the notion of *people* under the control of a clock seemed unnatural, even somehow blasphemous.

By the 20th century, however, it had become clear that there were important connections between the ticking of the clock and the workings of life, even within our own bodies. Scientists discovered that blood pressure varies naturally by time of day and began to think about issues such as sleep, hormonal cycles, and work

schedules, especially as industrialization and the modern age ushered in a 24-hour society dependent on shift work.

Still, chronobiology didn't begin to be recognized as a legitimate field of scientific study until around the 1960s, with the work of scientists such as Franz Halberg at the University of Minnesota, who coined the term "circadian" (meaning a 24-hour period), and Colin Pittendrigh at Princeton and Stanford, who organized the first dedicated scientific symposium on biological clocks at Cold Spring Harbor Laboratory in 1960. Halberg, Pittendrigh, and their colleagues helped to lay much of the foundations of chronobiology, weaving together different strands of inquiry from biology, psychology, and genetics.

Like many other interdisciplinary sciences arising from the intersection of more traditional fields, however, the nascent field still had trouble being taken seriously. "Back in the late '80s, a colleague of mine at Dartmouth, one of the premier circadian people, wrote a grant on circadian rhythms and one of the reviewers called it the field of 'spoon bending,'" notes Sehgal. "It was viewed as 'soft' science, it was not hard science, it was something that psychologists did." That finally changed when new techniques began to reveal the actual workings of biological clocks at the neurological and especially the molecular level – showing that they're much more complex and important than previously believed. "It wasn't until we started finding genes and molecules that people took it seriously."

"When I went to medical school, what I was taught was that the body had a clock, and the clock was in this part of the brain called the suprachiasmatic nucleus or SCN," recalls Mitchell Lazar, M.D., Ph.D., the Sylvan H. Eisman Professor of Medicine and director of the Institute for Diabetes, Obesity, and Metabolism. "And the way we interact with our environment was that light hits our retina, which is part of the brain, the retina sends a neural signal to the SCN that more or less says it's light out or it's not light out. That helps to entrain the clock in the SCN, and then through the peripheral nervous system and the nerves, the SCN tells the rest of the body what time it is, so it's coordinated. That was the old model."

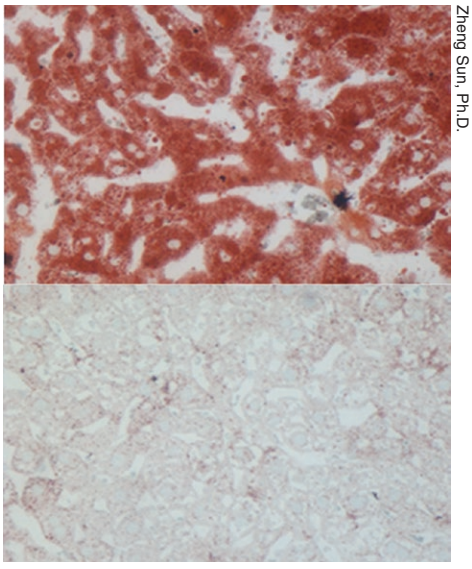
In essence, rather than being ruled by one big clock whose bell tolls throughout the entire organism, every living thing is a clock shop, containing a multitude of timepieces ticking away in unison – but not always in synchronization.

But it's not that simple. The SCN, about the size of a grain of rice and located in the middle of the brain in the hypothalamus just above the optic nerves, is indeed the neurological master clock in humans, governing the circadian rhythms that comprise the most important biological time cycle. Wired into the optic nerve, the SCN gets its cues about light and dark from the light receptors in the retina of the eye, then sends this information on to the pineal and pituitary glands and other parts of the hypothalamus. Hormones such as melatonin and cortisol are then released into the bloodstream to control physiological and behavioral responses such as body temperature and blood pressure, among many others.

Yet the SCN isn't the only clock in your body. In fact, virtually every one of your cells contains a molecular clock that controls its functioning and interactions with other cells and tissues. The same is true of essentially all other living things, down to the simplest and most primitive one-celled organisms like cyanobacteria. In essence, rather than being ruled by one big clock whose bell tolls throughout the entire organism like Big Ben in the streets of London, every living thing is a clock shop, containing a multitude of timepieces ticking away in unison – but not always in synchronization.

Just as rhythm is a fundamental part of music, it's also an essential part of life. But while it's quite possible to have music without rhythm, life is impossible without the presence of regular, recurring time cycles. There's the familiar 24-hour circadian cycle, which can be divided into diurnal (daytime), nocturnal (nighttime), or crepuscular (twilight) periods. But living things also follow other cycles: infradian (longer than one day), such as the human menstrual cycle or the migration patterns of some animals; ultradian (shorter than a day), such as sleep periods; and even cycles tuned to the ebb and flow of the tides. All living things dance to a variety of rhythms.

Those rhythms and the clocks that keep them are not arbitrary or random but are



Zheng Sun, Ph.D.

A research team led by Mitchell Lazar has discovered molecules that act as "shift workers" to maintain the daily circadian rhythm of fat metabolism. When those molecules do not do their jobs, the liver fills dramatically with fat, as shown in the top image of liver tissue. The bottom image shows tissue with normal levels of the molecules.

an inevitable result of our evolution on this particular planet. "It's a robust biology that evolved as a function of Earth's rotation on its axis relative to a star every 24 hours," explains David Dinges, Ph.D., chief of the Division of Sleep and Chronobiology in the Department of Psychiatry and associate director of the Center for Sleep and Circadian Neurobiology. Ultimately, he says, "chronobiology is based on orbital mechanics." If we ever discover life on another planet with a different orbital period and different days and months and years, that life will move to those rhythms, its biological clocks set to an entirely different time from our own.

Just as the elements that make up our bodies were once forged millions of years ago inside the hearts of exploding stars, we live by the rhythms of our planet and star. As Dinges puts it, "It's such a fundamental area of what it means to be a life form on Earth that it's difficult to imagine it not being involved in key ways to how we maintain our energy equation, our input-output equation, and therefore our health."

As Penn researchers are discovering, that elemental connection between our biological origins on Earth and how we live and thrive concerns far more than when we sleep or when we get hungry. When things are out of sync or out of communication, the rhythms of life and health can be fundamentally disrupted.

The 24-hour circadian cycle is the most important, because by definition it's the one we deal with every day. Sehgal has spent her career probing the molecular basis for that cycle, the so-called molecular clock, and how it triggers the need for sleep. She's managed to find some important pieces of the puzzle, including one of the genes involved in the molecular clock, and has identified some crucial signaling pathways that drive the circadian cycle.

"I got into this field when I was a postdoctoral fellow at Rockefeller University, where we discovered the second animal

Sabina Louise Pierce

Mitchell Lazar has demonstrated an epigenetic control of metabolism that is also circadian.

circadian rhythm gene," she says. "There was only one known in animals before that." That was back in 1994, after which, she explains, "the field sort of took off. Mammalian homologues were found and the mechanisms started being worked out."

Much of Sehgal's research involves the trusty fruit fly, *Drosophila melanogaster*. Although flies can't close their eyes like humans (nor do they dream, as far as we know), they sleep just the same, and Sehgal's lab has used the *Drosophila* model to find two genes also present in humans, *timeless* and *period*, that regulate the 24-hour cycle of rest and activity and how the cycle is reset by light.

Sehgal found that it was the levels of the *timeless* protein that varied with light and darkness. "The mechanism by which the clock resets in response to light is through reducing levels of the *timeless* protein. The protein's levels are high at night, low during the day. For many years people had known that if you shine light at night, you reset your clock." Meanwhile, the PER protein sets the length of the cycle. By tweaking the PER gene, Sehgal was able to actually alter the 24-hour circadian rhythm of the molecular clock to a 19-hour cycle. The experiment proved that, while it can be affected by light, the circadian clock is ultimately a genetic mechanism.

"In all species now where mechanisms regarding the response to clock have been identified, it's always a change in the levels of what we call a clock component, one of these gene products," she explains. "Circadian rhythm by definition is something that can persist in the absence of environmental cues. So if something goes up and down with a 24-hour rhythm in a light and dark cycle, it's not necessarily a

Years after **Mitchell Lazar** discovered the Rev-Erb molecule, his lab found that variations in the levels of Rev-Erb with the circadian cycle affected lipid synthesis in the liver. Disruption of the molecule led to a dramatic increase in liver fat in mouse models.

David Dinges, shown here with Andrea Spaeth, a graduate student, has extensively studied the effects of sleep deprivation.

circadian rhythm, because it could be driven by light. Circadian rhythms have to persist in constant darkness. However, they *can* be reset by light, and they usually are synchronized to your environment, which is why you suffer from jet lag when you go from one time zone to another."

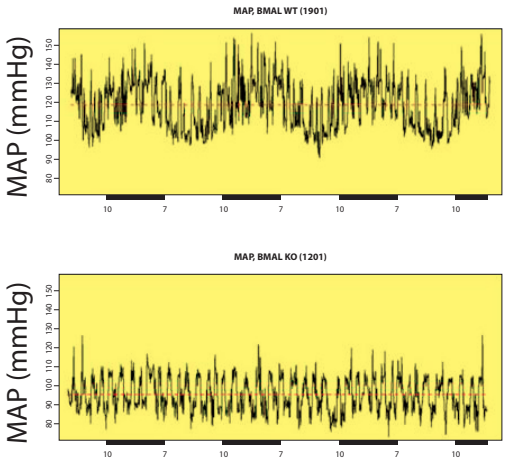
While the genetic mechanisms are complex and still not fully understood, it's not too surprising to think that something like our sleep and waking patterns would be intimately tied into biological clocks. Surprises have come on other levels, however. Sehgal notes that "in the past 10-12 years [it's become clear] that clocks are not restricted to the brain. There are clocks in many different body tissues, be it flies or mammals. So there's a clock in the liver, there's a clock in the kidney, there's a clock in the pancreas, and they're controlling local tissue specific functions. The fact that so many processes are rhythmic is something else that's been somewhat surprising. The extent of circadian regulation was not known until we actually realized there are clocks everywhere and then started looking more carefully and realizing that genes are cycling everywhere."

That discovery leads into the next surprise, which has been the increasing synergy that researchers are uncovering between body clocks and other vital biological processes that involve eating, fertility, metabolism, and maintaining the body's equilibrium. "About 10 years ago, using DNA arrays, we and other groups estimated that about 10 percent of genes in the body were under clock control," says John Hogenesch, Ph.D., professor of pharmacology in the Institute for Translational Medicine and Therapeutics at Penn. "Since then we've redone the studies with more sophisticated technology and experimental design, and now we're finding that over a third of the components of your genome, including more than half of all drug-response pathways, are clock-controlled. I think that reinforces what clock biologists have felt all along, which is that probably at least a third if not more of our physiology and metabolism is under either direct or indirect regulation by the clock."

As Dinges points out, "Food intake, heat retention, heat loss – these are part of the body's basic energy regulation and then behavioral activity. And the circadian system regulates all of these."

But how do those clocks work to control so much activity? How do they communicate with each other and the organs and tissues under their purview? How does the SCN in the brain coordinate and synchronize it all? These are the questions that researchers such as Garret FitzGerald, M.D., chair of the Department of Phar-

As **David Dinges** points out, "Food intake, heat retention, heat loss – these are part of the body's basic energy regulation and then behavioral activity. And the circadian system regulates all of these."



In mice with normal clock protein function, blood pressure rises during the morning hours (top). But Annie M. Curtis, Ph.D., and Garret FitzGerald, M.D., have demonstrated that in mice in which the clock gene has been knocked out, the daily variation in blood pressure vanishes (bottom).

macology and director of the Institute for Translational Medicine and Therapeutics, are investigating. He's found that communication between the SCN master clock and the body's peripheral clocks isn't just one way. "I've used the example of an orchestra," he says. "In an orchestra, the guy with the stick obviously communicates to the people playing the various instruments – he's the master clock. But his behavior is conditioned to some degree on the behavior of the person playing the oboe. And furthermore we have evidence now that peripheral clocks talk to each other as well. So the guy playing the violin is influenced by the guy playing the oboe. The dominant paradigm is the master clock, but it's a lot more complicated than that. And just like the guy playing the oboe, these peripheral clocks also have the capacity for autonomous behavior."

FitzGerald is particularly curious about the role of clocks in regulating metabolism. "We're obviously very interested in the degree to which gene variation in clock genes may contribute particularly to cardiovascular dysfunction and also to the metabolic syndrome, which is intimately linked to cardiovascular dysfunction," he says. Previous work by his laboratory isolated the cardiovascular clock and showed how it controls variations in blood pressure over time. "And when we went to look at the genes that oscillated in the aorta and that would be under the control of the clock, we were amazed to find that they fell into very discrete functional cassettes: carbohydrate metabolism, lipid metabolism, dipocyte maturation, and vascular integrity. And they're the elements that are disordered in metabolic syndrome. So here was for the first time a mechanistic integrator of the very discrete phenotypic expressions of metabolic syndrome. We went on from that to show that the clock played a very big role in carbohydrate metabolism."

Most recently, FitzGerald found a link between disruption of the clock and obesity – and, even more interesting, evidence that just as the master clock in the SCN directs the other clocks throughout the body, those peripheral clocks can also direct the SCN. Using his orchestra analogy, it's as if the oboist takes over the baton from the conductor in the middle of the symphony. When FitzGerald deleted an important clock gene called *Bmal1* in fat cells of mice, the SCN's own clock was disrupted. "We showed that this altered the signaling of lipids in the plasma that went through to the feeding centers in the brain to alter behavior in a way that resulted in obesity." The findings are consistent with previously well-established correlations between night shift work and sleep disorders with a higher risk for obesity and metabolic disorder.

Another component of the molecular clock with a connection to metabolism is a molecule called Rev-Erb, which exists in two forms (Rev-ErbA and Rev-ErbB). They are part of a family of molecules known as nuclear receptors which are master regulators of metabolism and development. Lazar notes that when he discovered Rev-Erb back in 1989, "it was an orphan, meaning that we really didn't know what it did. For many years my lab was studying it from the point of view of an interesting molecule that must have a function and we'd really like to know what it is."

Then another group in Switzerland discovered a strong correlation between variations of Rev-Erb levels and circadian rhythms, which led Lazar's lab to focus on just how Rev-ErbA and B fit into the molecular clock. They found that variations in the levels of Rev-Erb with the circadian cycle affected lipid synthesis in the liver. Disruption of Rev-Erb led to a dramatic increase in liver fat in mouse models. "These studies really for the first time dramatically demonstrate an epigenetic control of metabolism that's circadian and

Sabina Louise Pierce

Garret FitzGerald has found a link between disruption of the clock and obesity.

has physiological significance, because fat in the liver can be both a cause and effect of diabetes and it can also be a problem in terms of the liver itself," Lazar points out, adding that fatty liver is the second-most common reason for liver transplants.

As vitally important as all these natural clockworks may be to human life and all other organisms that have evolved on our planet, why did they arise in the first place? Why is it necessary to have any sort of built-in clock mechanisms?

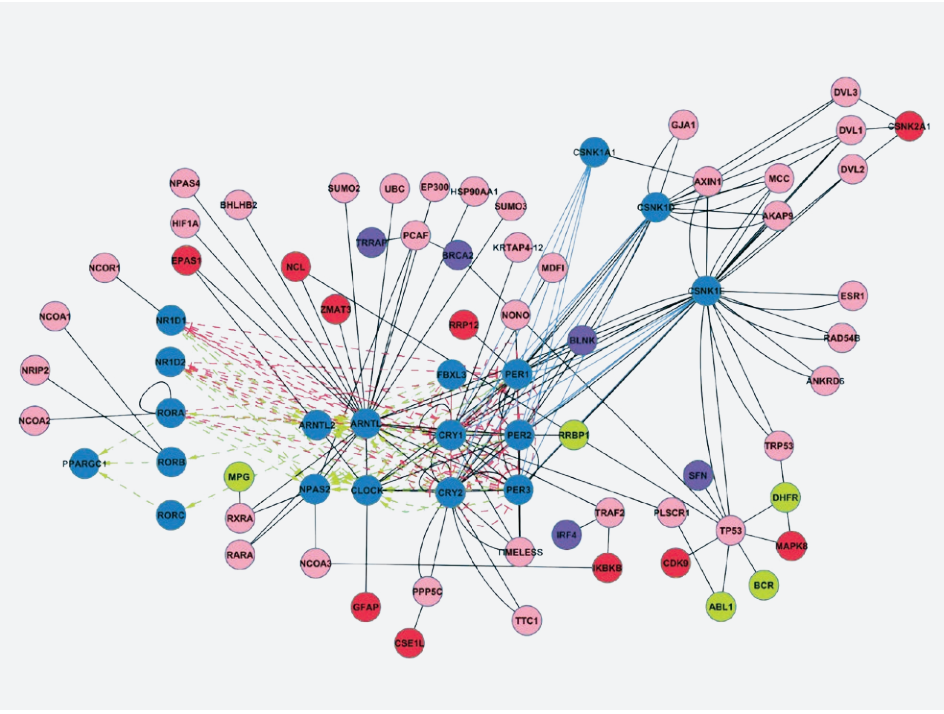
Albert Einstein once observed that "the only reason for time is so that everything doesn't happen at once." Hogenesch, who spends his time studying genetic clocks and the various physiological processes they control, tends to agree. "The way I like to think about it is, the clock functions in multicellular organisms as a way to temporally separate incompatible biochemistries. For example, you can't have oxidative and reductive reactions occurring in the same place and time. Tissues allow you to separate them by place, but the clock allows you to temporally organize things in a way that's more efficient. So the evolution of clocks may date back to needing to do these various chemical functions. In ancient organisms not having multiple tissues, temporal organization was the only way to do it."

Whatever the reason for our biological clocks and whatever many functions they may perform, it's quite clear that messing with them is never a good idea. According to Dinges, "Chronobiology is a hardwired, fairly inflexible biology, and yet social and economic systems of modern humans provoke it constantly." Anyone who's experienced jet lag, worked on a swing shift, or just missed a night or two of sleep can attest to that. "Sleep loss is only one piece of that provocation," Dinges adds. "Other pieces are this disturbed timing and ingestion of food at the wrong time, which can make you fatter faster. It may also make you more likely to be chronically sleep deprived and therefore less safe and less able to be alert. And then there are other unintended consequences we don't understand. There is evidence from the World Health Organization of higher rates of cancer – breast and prostate – with night-shift work."

Garret FitzGerald and his team have been "very interested in the degree to which gene variation in clock genes may contribute particularly to cardiovascular dysfunction and also to the metabolic syndrome."

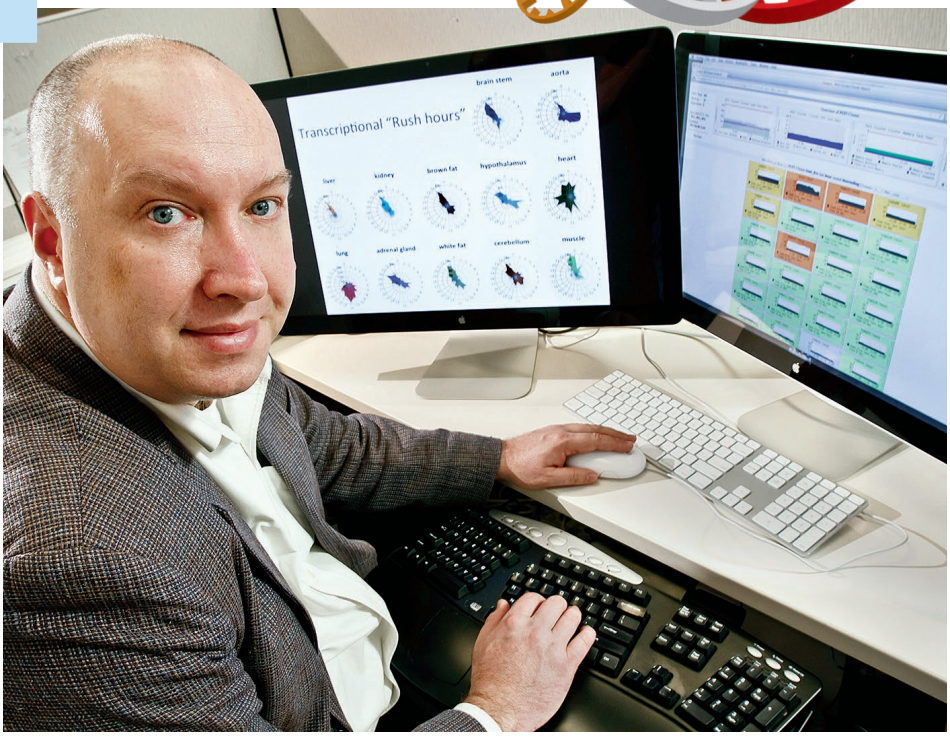
One aim of chronobiology, aside from simply understanding the whys and wherefores of our inner clocks, is to find ways to better adapt to and live with the inevitable disruptions that modern life imposes upon our natural and ancient biological rhythms. Dinges is working to develop mathematical models to better predict human circadian timing with an eye toward achieving greater harmony between nature and necessity. "These models are increasingly being used and looked at and evaluated and deployed in regulated industries around the world, industries where governments historically have regulated how many hours you can work – trucking, aviation, mining. And we're seeing that these models can help predict when workers are going to be at greater risk or which schedules are less dangerous or less problematic than other schedules."

Sehgal notes that a better understanding of the workings of the molecular clock and how it influences behavior and metabolism could also lead to drugs that could ease jet lag and the symptoms of sleep deprivation. The work of FitzGerald, Hogenesch, and Lazar on how clocks influence metabolism and other essential



John Hogenesch

The illustration conceptualizes the expanded clock gene network, showing clock-influencing genes that are involved in a large number of biological processes. Dozens of molecular pathways are functionally interconnected with clock function and vice versa.



John Hogenesch: "We're finding that over a third of the components of your genome are clock-controlled."

functions of the body could also have wide-ranging therapeutic implications. "For example, if we disable the clock, we have in mice a syndrome of accelerated aging, which suggests that sufficient clock function is very relevant to our biological equipoise," FitzGerald explains. "We know even from studies of humans that many of our hormones cycle through the day, and as we get older, those rhythms lose time before they eventually peter out. So I think there's a lot of interest in how clock dysfunction might contribute to aging and how that dysfunction is associated with so-called oxidative stress." FitzGerald also notes that the efficacy of drugs could also be improved by achieving greater harmony with the body's timekeeping: "It's been known for decades that time of day can substantially influence the kinetics of how drugs are broken down and eliminated. If you give the same drug at a different time of day, you may get very different drug levels, and therefore different responses. Despite that knowledge, it's remarkable how little it's influenced clinical practice."

By its very nature, because it involves so many different facets of life at their basic functional levels, chronobiology has developed as a decidedly interdisciplinary science. From a discipline that was once considered little more than "spoon bending," something soft and fuzzy and perhaps only just slightly more dignified than ESP research, it has blossomed into a vital field encompassing molecular biology, physiology, endocrinology, neurology, genetics, psychiatry, sleep studies – even astronomy, when one considers the cosmic origins of the biological clock. "It's so pervasive that's there's no one scientific society or group where you can see all this," Dinges observes. "You actually have to go to many meetings to see people working on this at many different levels. It reflects the many ways in which this system needs to be understood and probed and dissected and modeled."

Sehgal elaborates: "To some extent the interdisciplinary nature helps in figuring things out. You go to a meeting and there's going to be people studying cyanobacteria and people studying mice and flies and people studying humans, the whole gamut. The interdisciplinary nature has helped move it ahead."

The field's need for intellectual diversity and a range of different scientific viewpoints has made Penn a hotbed of chronobiological discovery. "I think it's a little bit accidental and a little bit because Penn is such a great place for collaborations," says Lazar. "We all have different angles that we take, which is good – we wouldn't want to be doing the exact same things. But it's very complementary. I think it's safe to say there's no internal competition here, which is really a fantastic aspect of this."

As Hogenesch puts it, "It highlights the incredible breadth and depth of researchers and research we have at Penn. I think it's a point of pride for our clock and sleep community here, the sheer excellence of the people here and how collaborative everyone is."

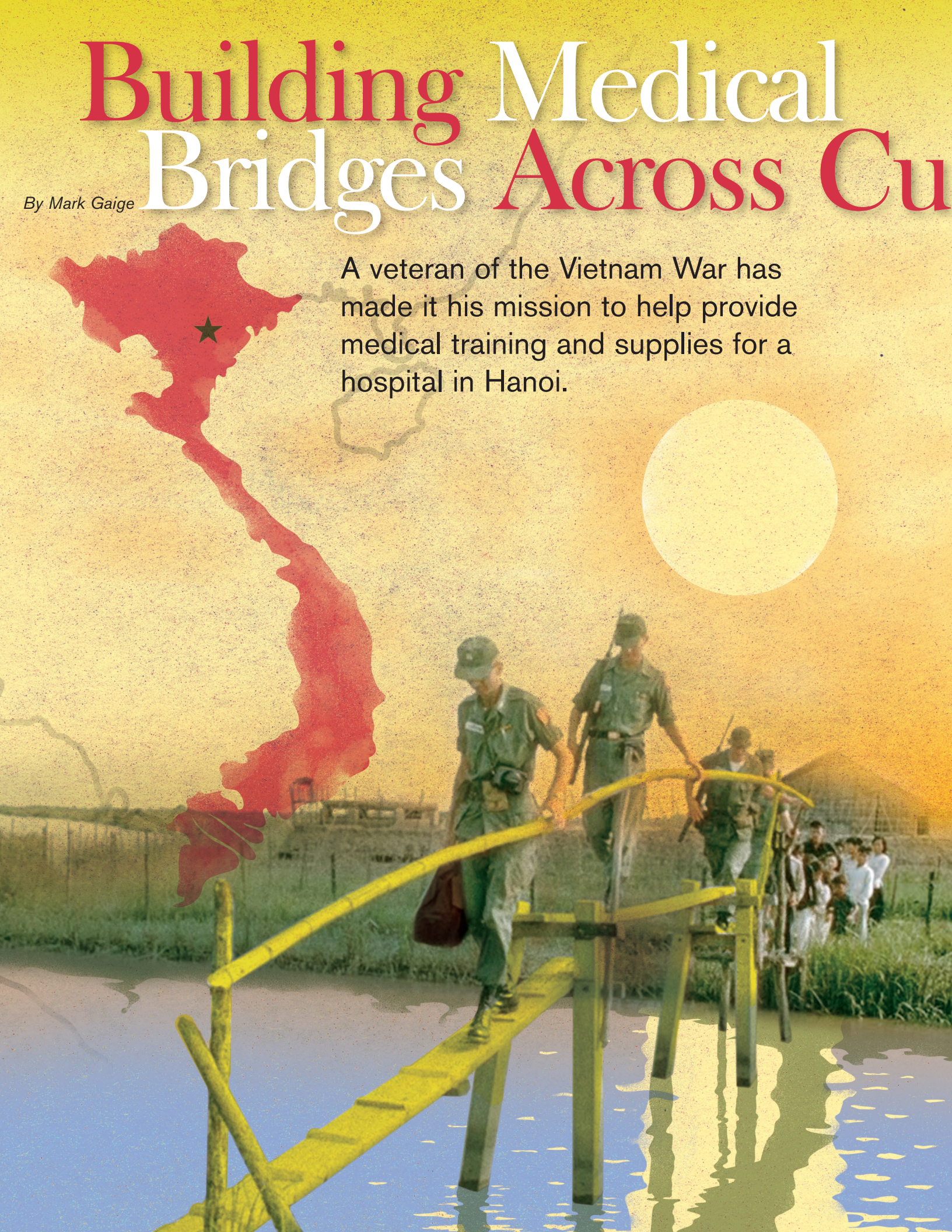
John Hogenesch views the clock functions in multicellular organisms "as a way to temporally separate incompatible biochemistries. For example, you can't have oxidative and reductive reactions occurring in the same place and time."

The questions of chronobiology are as intricate and varied as the pieces of a clock – the gears, the springs, the screws – and Penn scientists are working to put all the pieces together. We may not be able to escape the clocks that mark the moments of our lives, but we can learn to better harmonize with their rhythms. •

Building Medical Bridges Across Cu

By Mark Gaige

A veteran of the Vietnam War has made it his mission to help provide medical training and supplies for a hospital in Hanoi.



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As donations increased, taking supplies and equipment to Vietnam required a large plane.

Like many Americans who had once supported the war in Vietnam, Carl Bartecchi, M.D. '64, eventually became disillusioned with America's role in the conflict. "I read a good portion of the Pentagon Papers when they were released by the media in 1971," he recalls, "and it became clear that why I thought we were in Vietnam wasn't the main reason we actually were in Vietnam."

And when Bartecchi says "we," he means it literally. He was drafted by the U.S. Army in November 1964 while an intern at Henry Ford Hospital in Detroit. Eleven months later he would begin a one-year tour of duty as an army flight surgeon caring for U.S. servicemen in Soc Trang, a city of 40,000 in the Mekong Delta that housed a U.S. air base. The stint would change his life in more ways than one.

Bartecchi, today a distinguished clinical professor of medicine at the University of Colorado School of Medicine and practicing internist in Pueblo, Colorado, arrived in South Vietnam just as the American presence there was escalating. In March 1965, 3,500 Marines had been dispatched to the country, beginning the U.S. ground war. By December the number had swelled to nearly 200,000 troops.

While the dramatic growth in U.S. personnel placed, on occasion, a heavy, "almost unbelievable," demand on his skills as the only U.S. physician on the Soc Trang base, at other times there was nothing to keep him and his small team of medics occupied. But as Bartecchi says, "If doctors have nothing to do, we'll soon find some way to put our skills to good use." So that's what he did.

It wasn't long before he and the medics – whom he recalls as "a fantastic group of young enlisted men" – discovered a local orphanage that had almost no medical help. The children suffered from malnutrition, worms, skin infections, and other "diseases of the tropics." They had no meat or vegetables and usually ate only a single meal of rice each day. Bartecchi and the medics provided them with antibiotics, soap, and vitamins; other U.S. soldiers fixed the water supply. Soon word spread to the residents of the city and the medical team found themselves caring for them as well.

"The only medicine we ever saw was folk medicine," said Bartecchi. "And it didn't work." (His exposure to home-style remedies triggered a career-long antipathy to "naturalistic" medicine that resulted in the publication of his book *The Alternative Medicine Hoax* in 2000.)

Starting in 1995, "We brought defibrillators, pacemakers, stethoscopes, medicine – anything we could fit into one of the two suitcases that we were each allowed to bring into the country," Bartecchi recalls. Years later, he chartered a Boeing 747-400 to transport equipment and supplies to Bach Mai Hospital.

Seeing a huge, continuing need that was not being met, he decided to help further. So the young doctor obtained donations of medicine, pediatric vitamins, soap, clothes, and toys from charity organizations in the United States, coordinated their delivery into Vietnam, and organized non-government medical missions to the towns and villages. In addition to helping patients, the good will enabled U.S. personnel to establish trust with the Vietnamese.

After Bartecchi's return to the United States, he followed events in Vietnam closely. The 1972 Christmas bombings of

Hanoi (the capital of what was then North Vietnam), coming on the heels of the Pentagon Papers, inspired him to take action to help the people recover from the war's effects. As he puts it, "I found myself wanting to try and make life a little better for the civilians in Vietnam."

Because of the freeze in relations between the U.S. and Vietnam after the war ended, the opportunity to do so did not materialize for a quarter of a century. But shortly after diplomatic ties between the two countries resumed in 1995, Bartecchi and his wife, Kay, began the first of what would generally become twice-a-year visits to the country that continue to this day.

On each trip they would bring medical supplies for the Bach Mai Hospital in Hanoi. "We had learned that the hospital had great needs, so we tried to help. We brought defibrillators, pacemakers, stethoscopes, medicine – anything we could fit into one of the two suitcases that we were each allowed to bring into the country," he says. While in Hanoi, Bartecchi held educational sessions for Vietnamese physicians and soon began to recruit other U.S. doctors to lecture and train. Eventually he arranged for a number of Vietnamese doctors to come to the United States for additional training so they could return home to teach their colleagues. To date, more than thirty Vietnamese physicians have been trained at St. Anthony's Hospital in Lakewood, Colorado, and the Mayo Clinic as part of this effort.

Bartecchi has held educational sessions for Vietnamese physicians both in Vietnam and in the United States. For all of his humanitarian and educational efforts over the years, Bartecchi has been awarded an honorary professorship at Hanoi Medical University.

And then there's the equipment: Ventilators, hundreds of beds and mattresses (the 3,000 patients in the hospital used to have to squeeze into 2,000 beds), EKG and ultrasound machines, monitors, infusion pumps, Dopplers, cases of catheters, textbooks, CDs, spare parts . . . all solicited by Bartecchi from hospitals, fellow physicians, and medical supply companies and flown to Hanoi for use in the Bach Mai Hospital. The donations now total more than 50 tons of new and refurbished hospital equipment, learning materials, and supplies worth several million dollars.

Bartecchi reports that the patients and doctors are always very grateful for the donations. "I accompanied a major shipment that arrived this past October, and it was extremely moving to see their reactions."

That 50-ton delivery in October must have been a real scene. With the help of Chapman Freeborn, an airplane-leasing company based in London, and with donations from numerous individuals and organizations, Bartecchi chartered a Boeing 747-400 to transport the equipment. He recounts: "After we arrived at the hospital with truckloads of equipment and supplies at 5 a.m., we witnessed a circus-like atmosphere, with 190 beds and mattresses and a cornucopia of sophisticated equipment piled everywhere in the courtyard in front of the hospital and moving in every direction, led by hundreds of doctors, nurses, aides, and volunteers. A neurosurgeon came to claim his 16 beds and patient-monitors for a new neuro ICU. We saw beds being pushed, monitors being carried, and ventilators being pulled by smiling porters. The beds were wheeled to the halls outside the patient wards, cleaned and disinfected, then moved into the wards – to the delight of the surprised patients. The joyful expressions on their faces as they saw their new beds with good mattresses is something I will always remember. The ward staff then re-

turned to their regular routines, smiling as they tested the movements of the new electrical beds. The old beds were carted off to a bed graveyard in the back of the hospital."

A biomedical engineer from Bartecchi's home hospital accompanied him on the flight and spent the better part of a week helping assemble and test the various devices as well as teaching Bach Mai technicians how to maintain and repair everything. He also left manuals for all the machines and set up a communication program with the technicians.

The event was more poignant because of where it took place. The courtyard where the supplies were distributed is the site of a monument to the 28 Vietnamese doctors and nurses who died when an errant 500-pound bomb broke loose from a U.S. Air Force plane during a mission against a nearby military target in 1972. Says Bartecchi: "Though I was with several of the doctors who were there at the time of that disaster, none of them brought it up, having long ago recognized the futility of dwelling on the past and instead focusing on the need to work for the future."

Bartecchi's one regret? "I only wish that all of the people, organizations, and institutions that contributed so much equipment, time, and money to the effort could have been there to experience the joy and goodwill that their donations generated."

And there's more.

Bartecchi has written a book called *A Doctor's Vietnam Journal* (which was favorably reviewed in *The New England Journal of Medicine*) that recounts his experiences in the 1960s as a military doctor in that country. So far, more than $25,000 has been raised from royalties and donations from readers, all of which has gone straight to the Bach Mai Hospital project.

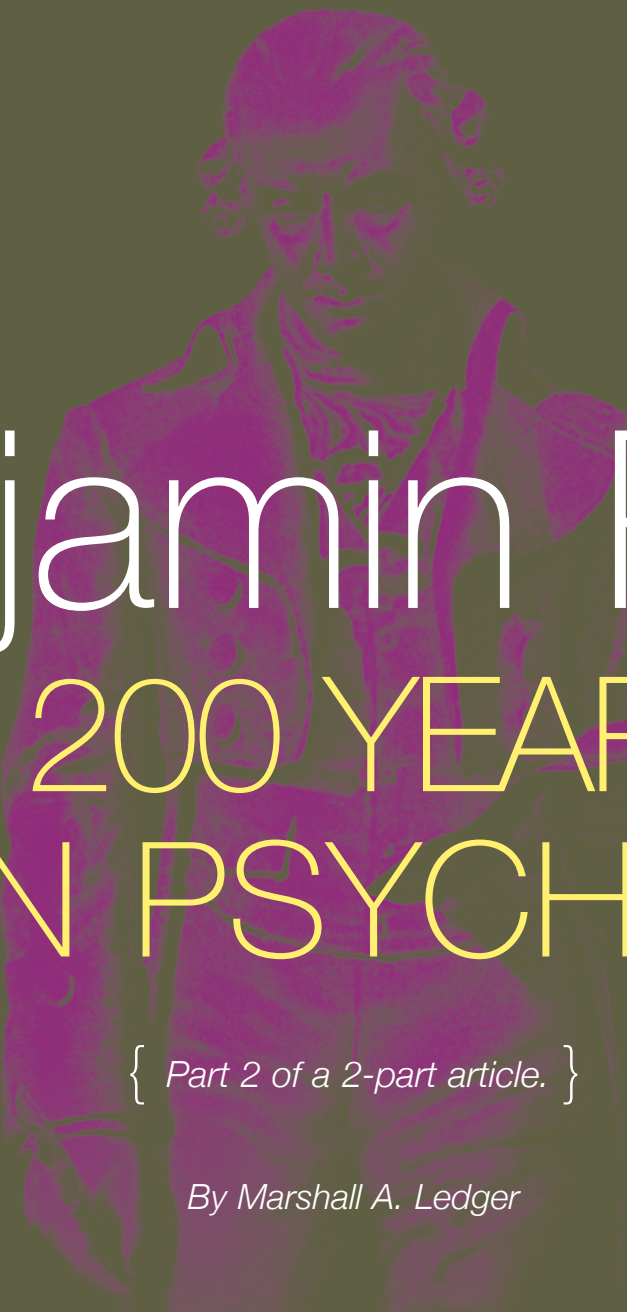
Bartecchi is also active in promoting the advance of new medical knowledge into Vietnam. A month after the massive October 2012 equipment delivery, the Third International Pediatric Symposium was held at the Bach Mai Hospital. Participants came from all over Vietnam. The symposium featured lectures by six pediatric specialists from the Mayo Clinic, most of whom were heads of specialty departments. One memorable moment came when a U.S. toxicologist who was part of the delegation encountered a patient who had serious breathing problems after being bitten on the side of the head by a green viper. A bronchoscope that was part of the October delivery was decisive in helping the toxicologist provide an airway for the patient.

Carl Bartecchi, left, with Ngo Guy Chau, M.D., Ph.D., Vice Director of Bach Mai Hospital.

For all of his humanitarian and educational efforts in Vietnam over the years, Bartecchi has been awarded an honorary professorship at Hanoi Medical University.

If running his own busy medical practice, teaching at the University of Colorado School of Medicine, and coordinating the Bach Mai Hospital project doesn't sound like it's enough to keep this very active physician as busy as he wants to be . . . you're right. That's why Bartecchi also writes a weekly health column for the *Pueblo Chieftain* (his hometown paper), continues to volunteer his services at the migrant worker clinic he founded, and has published several medical texts and numerous articles in medical journals.

A recent editorial in the *Chieftain* entitled "The Good Doctor" saluted Bartecchi as "the wise and respected Pueblo physician" known for his "generosity of spirit." It concluded that "Pueblo can take pride in his work." Few who know him or who have benefited from his compassion – in this country or in Vietnam – are likely to disagree. ■



Benjamin Rush AND 200 YEARS OF PENN PSYCHIATRY

{ *Part 2 of a 2-part article.* }

By Marshall A. Ledger

In the years following the publication of Benjamin Rush's seminal book *Medical Inquiries and Observations, Upon the Diseases of the Mind* (1812), the field of psychiatry was slowly developing. But in 1909, S. Weir Mitchell, M.D., Philadelphia's most famous physician and a trustee of the University of Pennsylvania for 35 years, proclaimed to his neurology colleagues: "Amid enormous gains in our art, we have sadly to confess the absolute standstill of the therapy of insanity and the relative failure, as concerns diagnosis, in mental maladies. . . ." It was in the 1930s when the situation began to improve, at Penn and elsewhere, and psychiatry began to move increasingly into the mainstream.

Psychiatry at Penn entered the modern era when it – literally – entered the University catalogue. In 1931-32, the word *psychiatry* first appears as a "subject of instruction," with a faculty of nine, including one full professor. There was also an emeritus professor, Charles W. Burr, M.D. 1886, the former chair who was originally appointed a professor of "mental diseases."

The one active full professor was Earl D. Bond, M.D., who previously held the same title in the Graduate School of Medicine. Bond won the Philadelphia Award in 1932 for his work in founding the Institute of Pennsylvania Hospital, which opened in 1930. He also wrote, among other books, *One Mind Common to All* (1958), a lay discussion of mental illness, and a biography (1947) of Thomas S. Kirkbride, M.D. 1832, author of the highly influential *On the Construction, Organization, and General Arrangements of Hospitals for the Insane*.

In the University catalogue for 1932-33, psychiatry gets a chair, Edward A. Strecker, M.D., along with a faculty of 12. Strecker had already made a name for himself, according to medical historian Hans Pols, Ph.D. 1997: In 1928, Strecker and a colleague "first advocated the establishment of a licensing board for psychiatrists"; the American Board of Psychiatry and Neurology was founded in 1934.

Strecker was known for optimism about the field's potential, including psychotherapy. He and Bond made an ideal team, because both believed that quality of care could improve with better teaching and research. In an early venture, they lent money to a new clinician, Kenneth E. Appel, M.D., Ph.D., to travel abroad and be analyzed by Otto Rank, a close associate of Freud. (Appel reportedly was the first Philadelphia psychiatrist "to complete a personal analysis," said Francis J. Braceland, M.D., in a memorial article. Rank later visited Penn to teach.)

Disorders of Everyday Life

Strecker was called "one of the first, if not the first" to treat the disorders of everyday life. Along with Bond, he revived the dilapidated outpatient clinics at Pennsylvania Hospital, which had been built in 1885 as the first of their kind in the United States. They were geared to provide early treatment and offer preventive measures so that minor disorders would not advance to psychoses. In 1946, Strecker started an outpatient clinic at the Hospital of the University of Pennsylvania, with Appel in charge.

One of Edward Strecker's topics was doting "moms."

To Strecker, psychiatry was not a cloistered endeavor. His 1940 book *Beyond the Clinical Frontiers* made the case for psychiatry's place within all of medicine and society by offering "some helpful social applications of psychiatry and mental hygiene" in a world full of "economic, political, social, cultural, and ethical upheavals." He was particularly adept in addressing lay audiences and had a regular column in *The Saturday Evening Post*, where he wrote about not only illnesses but also normal family relations.

His bestselling book *Their Mothers' Sons: A Psychiatrist Examines an American Problem* (1946) criticized, as its jacket noted, the "millions of well-meaning and unthinking 'Moms' who will not cut the apron strings between them and their sons." They created, he wrote, a nation of immature, maladaptive men and even could have led to a military defeat in World War II: Strecker claimed that more than two million American men were rejected or

Penn University Archives

Four leaders in psychiatry at Pennsylvania Hospital and its Institute: from the left, Edward Strecker, Lauren H. Smith, Earl D. Bond, and Kenneth E. Appel.

Earl D. Bond, M.D., before a bas relief of himself, Edward Strecker, and Kenneth Appel. All had been presidents of the American Psychiatric Association. The bas relief was done by a former patient.

discharged from wartime service because of psychiatric issues.

Betty Friedan lumped Strecker among those who wanted to restrict women's activities to the home, and some historians have said that he helped fuel the consequent "pathologization of motherhood," attacks on what was disparagingly called "mother love" (for daughters as well as sons). Most recently, however, his reputation has been somewhat restored. In *Mom: The Transformation of Motherhood in Modern America* (2010), Rebecca Jo Plant, Ph.D., says that Strecker had "a lasting impact" on the question of a woman's place in the world, although, she adds, he was not strident about domesticity and suggested that women could avoid so-called momism "so long as they enjoyed a healthy marital sex life and cultivated other interests as their children grew older."

To Strecker and Bond, the way to improve the discipline meant not merely to add faculty and teaching hours but, as Pols points out, "to restructure the entire medical curriculum around a psycho-biological conception of patients as integrated personalities challenged by the social and cultural environments rather than as containers of more or less diseased organs."

Together, they established Penn's first credible psychiatry program for medical students: in the first year, lectures on personality development and problems; in the second, lectures on clinical psychiatry; in the third, clinical demonstrations; and then work on the wards of Philadelphia General Hospital and the Institute. As noted by John Paul Brady, M.D., a former chair of psychiatry at Penn, and the other editors of *Psychiatry: Areas of Promise and Advancement* (1977), the study of psychiatric disorders was finally tied into the preclinical sciences, general medicine, and the practical experience of managing patients.

Students became excited about the field even beyond the courses. The campus-based Strecker Psychiatric Society lent books and sponsored guest speakers not only on mental disorders but also on "the ever-widening area of psychiatric influence in general medicine and the specialties," according to a tribute to Strecker on his retirement. The lectures that the organization sponsored were so popular – medical students and others from all over the city attended – that cards of admission were issued.

Strecker was fully aware of the change in his discipline. In his presidential address to the American Psychiatric Association in 1944, the organization's centennial year, he noted that psychiatry had finally been admitted into the medical profession's "family circle."

The Avon Lady

Appel succeeded Strecker as chair, and he, too, thought expansively about psychiatry. When earning his advanced degrees at Harvard University, he had assisted in a course on psychopathology in Shakespeare. Early in his career, he collaborated with Strecker on the book *Discovering Ourselves* (1931), a practical guide for anyone giving or seeking counseling for emotional disturbances.

Appel tried to instill practice skills early. He created the "Family Health Advisor Service," in which medical students were assigned a family and served as its initial medical resource for their student years. It offered the best kind of teaching, "contact with actual situations," he said. "Thus the student is offered experience in the broad and basic aspects of psychiatry – where medicine, public health, social work, and psychiatry have common ground."

One of the department's residents, Karl Rickels, M.D., received a lasting lesson from Appel himself. As Rickels recalled in his 2011 memoir, *A Serendipitous Life*:

"I had examined a female patient in her forties for fifty minutes and had gotten nowhere. Dr. Appel came in and joined us and asked the patient not about possible symptoms or why she came to the clinic, but simply about her life. Her face lit up, and she told him that she was a part-time Avon sales lady. Dr. Appel asked her what products she had with her, and on the spot he bought something for Mrs. Appel. Within

ten minutes he found out what events led to her being sent to the clinic."

Appel also had national goals for psychiatry. He spoke out powerfully and frequently for improved care for patients in state hospitals, and, as head of the American Psychiatric Association in 1953-54, he based his presidential address on that theme.

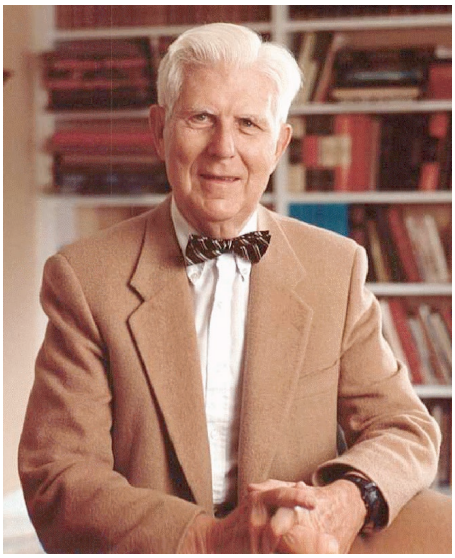
His efforts helped lead to the creation of the congressional Joint Commission on Mental Illness and Health, whose 1961 report, "Action for Mental Health," resulted in legislation that "was to bring the treatment of mental ills and mental retardation back into the mainstream of American medicine and to return the care of mental patients to the community," as Braceland wrote in his memorial to Appel. In 1963, the year the federal legislation was enacted and the last year of his chairmanship, Appel wrote that the extramural activity of hospitals in the community "is one of the new developments which has undreamt-of potentials."

Under Appel, the department's clinical research arm spiked. A cadre of his junior professors went on to garlanded careers – and they remain active in the department of the 21st century.

Beck Founds Cognitive Therapy

Penn's Department of Psychiatry has enjoyed remarkable continuity over the past half-century, due partly to several faculty members whose careers span that entire time. Among them is Aaron T. Beck, M.D., emeritus professor of psychiatry, who developed cognitive-behavioral therapy. According to the citation from the Albert Lasker Clinical Medical Research Award, which Beck won in 2006, the therapy "has transformed the understanding and treatment of many psychiatric conditions, including depression, suicidal behavior, generalized anxiety, panic attacks, and eating disorders."

Beck was practicing psychotherapy in the 1950s when he observed that his depressed patients were not expressing anger outwardly, as Freud described. Instead, as the Lasker citation noted, they drove it inward and felt "like losers." Exploring this idea, Beck found that "a patient's [own] beliefs, thoughts, or expectations generate distress." Could they do the opposite? The power of cognitive-behavioral therapy "derives in part from the fact that patients assume an active role in their recovery; as a result, they carry tools away from the therapist's office with which they can handle subsequent experiences that threaten their emotional well-being."



Aaron T. Beck, M.D.

Beck also developed ways to measure the severity of psychiatric symptoms, including a Depression Inventory, Cognitive Insight Scale, Hopelessness Scale, Anxiety Inventory, and Suicide Intent Scale. Among other benefits, they are credited with aiding the classification, assessment, prediction, and prevention of suicide.

Beck's explorations were not always appreciated. As Daniel Smith wrote in *The American Scholar*, the American Psychoanalytic Institute once rejected his membership application "on the grounds that his mere desire to conduct scientific studies signaled that he'd been improperly analyzed."

In general, however, Beck has been showered with awards. For example, he was elected a member of the Institute of Medicine of the National Academy of Sciences and a fellow of the American Academy of Arts and Sciences. And his name appears at or near the top of many a list of the most notable psychiatrists in the world. He remains active in various centers focused on continuing research and therapy based on his discoveries.

Karl Rickels: Serendipity and Focus

Karl Rickels, M.D., G.M.E. '57, the Stuart and Emily B. H. Mudd Professor of Behavior and Reproduction, entered psychiatry just as medications were emerging as treatments and quickly grasped their potential. His main interest has been non-psychotic patients with anxiety or depression – not only the drugs they take but also the role of non-specific factors in helping them recover.

With few guideposts for randomized clinical trials of drugs and placebos in anxiety and depression, Rickels developed his own methodologies. He moved his projects from hospitals into general-practice settings, where the illnesses "are primarily present and recognized," he wrote in *A Serendipitous Life*. "This development served as a model for today's multicenter trials in psychiatry and was a forerunner, by decades, of today's interest in effectiveness research in the community."

The National Institute for Mental Health supported Rickels's

work for 51 consecutive years, with a notable return on investment. His major achievements include a landmark study on medications to treat anxiety, published in *JAMA* in 1959; ground-breaking studies on the placebo response; the contribution of non-specific or non-drug factors to drug and placebo treatment; evidence for the effectiveness of antidepressants to treat generalized anxiety disorder; and seminal research on the drug imipramine, which led to a new generation of antidepressants.

The Food and Drug Administration has designated many of Rickels's studies "pivotal trials" leading to FDA approval of particular medications. Most recently, following the scientific findings of Irwin Lucki, Ph.D., G.M. '81, professor of psychiatry and pharmacology, and his team, Rickels led the trial that brought about FDA approval of vilazodone to treat adult depression, the first new antidepressant in a decade.

Rickels has also led studies that exposed the lack of effectiveness of many commonly used, over-the-counter medications and called attention to the risks of medication, such as dependence on benzodiazepines, a class of medication prescribed by physicians in almost every specialty. He studied the nature of the dependence and then described ways to both treat it and prevent it.

Last year, with his department's resounding support, Rickels won the Pioneer in Psychopharmacology Award from the International College of Neuropsychopharmacology.

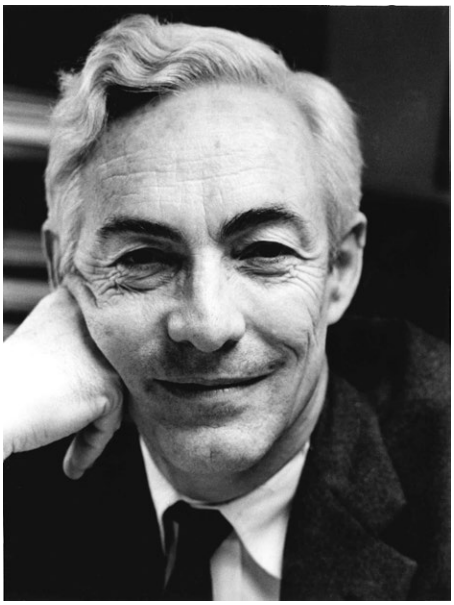
And he continues his work, studying the psychological aspects of infertility and the pathophysiology and treatment of premenstrual symptoms in a program based in the Department of Obstetrics and Gynecology as well as conducting research in the Mood and Anxiety Disorders Treatment and Research Program, which he founded.

Albert Stunkard's Modest Proposals

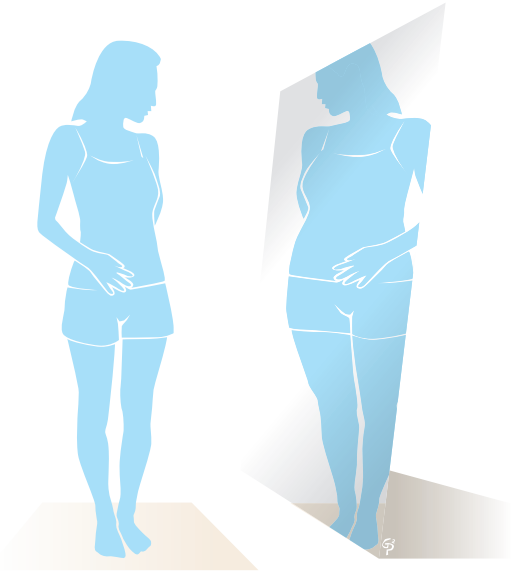
Albert J. Stunkard, M.D., who succeeded Appel as chair of psychiatry in 1962 and led it until 1973, is known for his research on obesity and eating disorders, their genetic, psychological, and environmental causes, and the development of therapies.

Stunkard identified binge eating. He also described night eating syndrome and developed a treatment for it. The disorder, also called "midnight hunger," involves, as he has written, "a delay in the circadian pattern of eating that disrupts sleep"; it also has a genetic component and mood fluctuations. It has been proposed for inclusion in the next edition of the *Diagnostic and Statistical Manual of Mental Disorders*, to be published this year (the only eating disorders currently recognized are anorexia nervosa and bulimia nervosa).

To Stunkard, obesity is not a simple problem, but it was thought to be so when he began his career. In the 1950s, psychotherapy, the era's preferred mode of treatment, was categorical about what obesity was: "the presenting symptom of a basic personality problem or disorder," as Stunkard put it in 1988 in the prestigious



Albert J. Stunkard, M.D.



Thomas W. Salmon Lecture sponsored by the New York Academy of Medicine. "In retrospect," he continued, "it is clear that it tried to explain too much too soon. It was impatient with the modest, low-level kind of inquiry more appropriate to our field."

He explained: "The major development of the past 30 years in American psychiatry seems to me to have been the rise of such modest empirical inquiry. In the process, psychiatry has become a cumulative discipline. We can now build on previous findings in a manner that was hardly possible in the 1950s."

For instance, the finding that obesity runs in families: so simple it had been ignored, yet now is "the starting point for research," he said. Yet, he was careful to add, genes are not destiny, but "a vulnerability, a liability, which requires a suitable environment in order to be manifested."

Accordingly, Stunkard has investigated both genetic and environmental influences on human obesity, using, among others, twins, adoptees, members of different social classes, and the Old Order Amish. For the past 18 years, he has been conducting a large-scale prospective longitudinal study of the growth and development of children at high risk of obesity. He and his team conducted a pilot study of cognitive-behavioral therapy with night eat-

ing syndrome; the results were significant enough for them to call for a controlled treatment trial.

In 1983, he developed the Stunkard Figure Rating Scale, which gauges the perception a person has of his or her body image. Other clinical investigators have tested it repeatedly and continue to find it valid and reliable. He founded Penn's Center for Weight and Eating Disorders; its related program in weight management is now named for him, as is the department's annual award for teaching and mentoring residents, in honor of his own support of house staff. He is a member of the Institute of Medicine.

Continued Excellence

The next generation of faculty members carved out their own distinctive niches. George E. Ruff, M.D. '52, emeritus professor of psychiatry, was "psychiatrist to the astronauts" – the only civilian psychiatrist to examine and advise the space travelers in Project Mercury (1959-63).

Charles P. O'Brien, M.D., Ph.D., G.M.E. '69, the Kenneth E. Appel Professor of Psychiatry and a member of the Institute of Medicine, started what is now the Center for Studies of Addiction/Treatment Research Center in 1971; its clinical center is named for him. President George H. W. Bush paid a visit in 1991, toured the research labs, and noted its robust capabilities. "It's not simply on interdiction; it's not simply on treatment. . . . It's across the whole sphere of the drug problem," Bush noted, adding,

Photograph by Candace diCarlo

Edna B. Foa, Ph.D.

"You combine the best in treatment – medical, social, and psychological – with this innovative research."

David F. Dinges, Ph.D., G.M. '79, professor of psychology in psychiatry, applies his expertise in sleep and chronobiology to everyday issues such as sleep disorders and sleep debt – and the usefulness of naps. He also studies behavior and performance in space flight, for which he has won the National Aeronautics and Space Administration's highest civilian honor. (See *Penn Medicine*, Fall 2012.)

Edna B. Foa, Ph.D., professor of clinical psychology in psychiatry and director of the Center for the Treatment and Study of Anxiety, focuses her work on obsessive-compulsive disorder, post-traumatic stress disorder, and social phobia. For combat-related PTSD, she developed the therapy of prolonged exposure, or PE: Patients identify the thoughts and situations that trigger their trauma, actively recall its circumstances and their memories of it, and perhaps revisit the site where it took place. "Facing the memories strips them of power. The approach not only works; it works fast – usually within 12 sessions," wrote Jeffrey Kluger in *Time* magazine, which in 2010 named Foa one of the 100 "most influential people" in the world.

Pulling It All Together

Despite many islands of prominence in the past, the department, reflecting the field as a whole, lacked cohesiveness: "Incoherence was universal in American academic psychiatry" in the 1970s-'80s, noted Paul R. McHugh, M.D., chair of psychiatry at Johns Hopkins School of Medicine, in a 2001 memoir.

The situation at Penn began to change when Peter Whybrow, M.D., became chair in 1984. He reorganized the department, combining clinical, research, and educational activities and restructuring resident training.

Whybrow also developed new laboratory space, revived HUP's inpatient unit, and developed a clinical neuropsychiatric diagnostic unit that incorporated labs involving brain and behavior, clinical psychoendocrinology, and chronobiology. HUP was possibly the first hospital to bring these components into one comprehensive

George E. Ruff, M.D., examined astronauts in Project Mercury.

service. Advances in neurosciences and increased specialization in psychiatry finally – after a century of wishing – made interdisciplinary research possible.

Dwight L. Evans, M.D., the Ruth Meltzer Professor who succeeded Whybrow in 1997, has significantly expanded on these efforts. The department, he points out, is tied into many medical center settings – for example, the AIDS clinic, transplant surgery, the Division of Sleep Medicine, and the Abramson Cancer Center. Caryn Lerman, Ph.D., the Mary W. Calkins Professor of Psychiatry and the Annenberg School for Communication, is the center's deputy director (she is a member of the Institute of Medicine, with expertise in nicotine addiction). As Evans puts it, "It's extraordinary for psychiatry to have that much involvement."

Photograph by Candace diCarlo

Today's department has greatly expanded services to patients.

The department also participates in all of the components of the Penn Compact, the program instituted by Amy Gutmann, Ph.D., when she became president of the University of Pennsylvania. The compact entails ground-breaking research, interdisciplinarity, and local and global engagement. One of the most notable components of the interdisciplinary research arm is known as Penn Integrates Knowledge, or PIK, where the department is represented by Adrian Raine, D. Phil., a University Professor and the Richard Perry Professor of Criminology, Psychiatry, and Psychology; his work emphasizes the neurobiological and biosocial bases of antisocial and violent behavior.

As an example of pioneering research, Evans mentions the new Neuroscience of Behavior Initiative, directed by Brian L. Strom, M.D., M.P.H., the George S. Pepper Professor of Public Health and Preventive Medicine. The $16.3-million project covers basic, translational, clinical, and population research in addiction, depressive disorders, and neurodegenerative disease.

In local engagement, Evans notes, the department rebuilt the inpatient units at Pennsylvania Hospital and relocated HUP's units there (they are all centered where they began more than two centuries ago). And the department extends its reach as an academic community health center through several programs: the Hall-Mercer Community Behavioral Health Center at Pennsylvania Hospital; new clinical services at the Penn-Presbyterian Medical Center; and a Mobile Clinical Trials Unit and Mobile Assessment Unit, through which vans help West Philadelphia residents participate in, and complete, the testing of HIV vaccines and other preventive measures.

Globally, as part of the Botswana-UPenn Partnership, directed by Harvey M. Friedman, M.D., professor of medicine and chief of infectious diseases, the psychiatry department is helping to develop a clinical clerkship in psychiatry for a new medical school in that country. In his Chairman's Report in the department's newsletter in 2009, Evans mentioned research and educational initiatives in all seven continents, even Antarctica ("You thought we couldn't possibly be here," he quipped). In an interview, he adds, "More than global," reflecting on Dinges's NASA-funded study on the International Space Station.

Expanding the Clinical Branch

The department's clinical branch is Penn Behavioral Health (PBH), directed by Rosellen Taraborrelli (she is also the department's chief operating officer and executive director of the Penn Medicine Neuroscience Center). PBH began in the late 1990s, Taraborrelli explains, when insurers were removing mental health from their plans and reducing fees for psychiatric services. It has grown to receive more than 80,000 outpatient visits annually – about half involving patient-oriented studies and clinical trials. That is more than double the number treated by department clinicians when Evans arrived at Penn.

Through PBH, Evans has bolstered the department's clinical offerings. New patient services introduced during the last seven years alone include addiction (the Charles O'Brien Center for Addiction Treatment), weight and eating disorders (the Albert J. Stunkard Weight Management Program), women's mental health (the Penn Center for Women's Behavioral

Penn Behavioral Health, begun in the late 1990s, has grown to receive more than 80,000 outpatient visits annually – about half involving patient-oriented studies and clinical trials.

Illustration by Mandy Newham

Wellness), family care (the Center for Couples and Adult Families), and anxiety and repetitive behavior disorders in children (the Child/Adolescent Obsessive Compulsive Disorder, Tics, Trichotillomania, and Anxiety Group). Other added services include transcranial magnetic stimulation, comprehensive consultation services for mood disorders, psychosomatic medicine, forensic psychiatry, geriatric psychiatry, and adult developmental disorders. Many of these specialty services are fully integrated with innovative research programs.

Penn Behavioral Health also has a corporate-services component: managing the behavioral health benefits for a large part of the University and the entire Health System and providing services to both employees and management in some 60 companies in and around Philadelphia, including the city's police department. As Taraborrelli points out, employee assistance ranges across the stressors of ordinary life – helping individuals cope with legal, financial, child-care, and elder-care issues, problems at work, or "sad-adverse" events, such as a death in the family. Management training helps a company's leaders deal more effectively with the behavioral factors of employee concerns. Says Evans, "I'm not aware of any other department that has developed that kind of program."

Evans points out other barometers of departmental success. Research awards, about $21 million a year when he arrived, now total more than $73 million annually, including American Recovery and Reinvestment Act stimulus grants. The National Institute of Mental Health has chosen Penn for a Clinical Research Scholars Program, which fosters the interest and expertise of two residents in each class in psychiatric clinical research. And the department ranks high in satisfaction among both residents and students.

Psychiatry and Neuroscience

Another example is the Penn Medicine Neuroscience Center, which Evans co-directs with Amita Sehgal, Ph.D., the John Herr Musser Professor of Neuroscience. Its strategy, set forth in 2011, describes four areas of research opportunity: neural repair, development and function of neural circuits, neural plasticity, and neuroimaging. And in all of them, Evans points out, psychiatry has an innovative role.

For instance, Raquel E. Gur, M.D. '80, G.M.E. '84, Ph.D., the Karl and Linda Rickels Professor of Psychiatry, uses neuroimaging to identify risk factors in very young children that may emerge as mental disorders in childhood or adolescence and continue into adulthood. She is collaborating with Hakon Hakonarson, M.D., Ph.D., associate professor of pediatrics, at The Children's Hospital of Philadelphia.

In this project, some 10,000 children and adolescents whose genotypes were already on record at CHOP were assessed behaviorally, or phenotyped; some 1,000 of them are being followed for several years. The data will be combined, giving researchers rich information on the behavior of developing brains and the role played by genetic factors. The study may help direct treatment and also be the basis for further research – "the convergence of clinical and basic neuroscience with genomics," noted Gur in the center's newsletter.

Evans compares the study's scope to the Framingham Heart Study, which has provided long-term prospective studies of cardiovascular disease. Gur's work "will help us understand genetically and behaviorally all sorts of conditions that may relate to mental illness – and perhaps to many other medical conditions as well," he says, adding, "It speaks to the future, to be sure."

Meanwhile, Evans tends to his department as well, determined to keep it and its multifarious initiatives united, informed, and enthusiastic. He praises a voluntary clinical faculty of more than 100, who teach and mentor at least one hour a week and serve on committees. He brings residents and senior faculty together for "masters dinners" at his house, where they can connect informally. And he produces a regular newsletter, *Penn Psychiatry Perspective*, to keep everyone up to date. Decades from now, the present-day history of the department will already be well detailed in its pages. ●

Marshall A. Ledger, Ph.D., is author, with David Y. Cooper III, M.D. '48, of *Innovation and Tradition at the University of Pennsylvania School of Medicine* (1990) and founding editor of *Penn Medicine*. For this article he acknowledges the substantial help of the University Archives and Records Center.

When Art Meets Science

Lili Guo, a Ph.D. candidate who studies cell death and neurodegenerative diseases, often turns to art to balance her life.

By Karen Kreeger

Frank Oppenheimer, founder of the well-known science museum in San Francisco, the Exploratorium, once described artists and scientists as "the official 'noticers' of society." As he put it, "they notice things that other people either have never learned to see or have learned to ignore – and communicate those 'noticings' to others."

Lili Guo, a Ph.D. student in the lab of Xiaolu Yang, Ph.D., in the Department of Cancer Biology and Abramson Family Cancer Research Institute, is definitely one of these "noticers."

Art is in her genes. So is science.

Guo comes from a family of artists. Her father is a professor of lithography and her mother is a graphic designer for a major publisher, both in China. She has been doing art in many forms since she was five and has been trained in many classical forms. "It has been part of my daily life since I was very young."

Despite this family influence, she says, "I thought I would be following a family tradition and become an artist, but I was

In "Metabolic Dysregulation Determines Senescence," Guo salutes Joan Miro. The clock on the left points to cells at different stages of aging.

always interested in science and did well in it. I thought art would be my career and that science would be my hobby, my side line. I realized if I pursued art, though, I couldn't do science, in China." As it turned out, however, "I could never leave science behind."

To keep art in her life, she designs cover images for journal articles for Penn faculty, bringing the relatively unseen inner workings of cells to life. She started when Dr. Yang asked for her help in coming up with a cover for a paper about tRNA in *Molecular Cell* in 2010. The cover was published, she says, "and we were all very excited."

Although she works in a cancer biology lab, her biomedical studies center on a protein's role in cell death and neurodegenerative diseases – specifically, how it protects the health of neurons during protein quality-control processes.

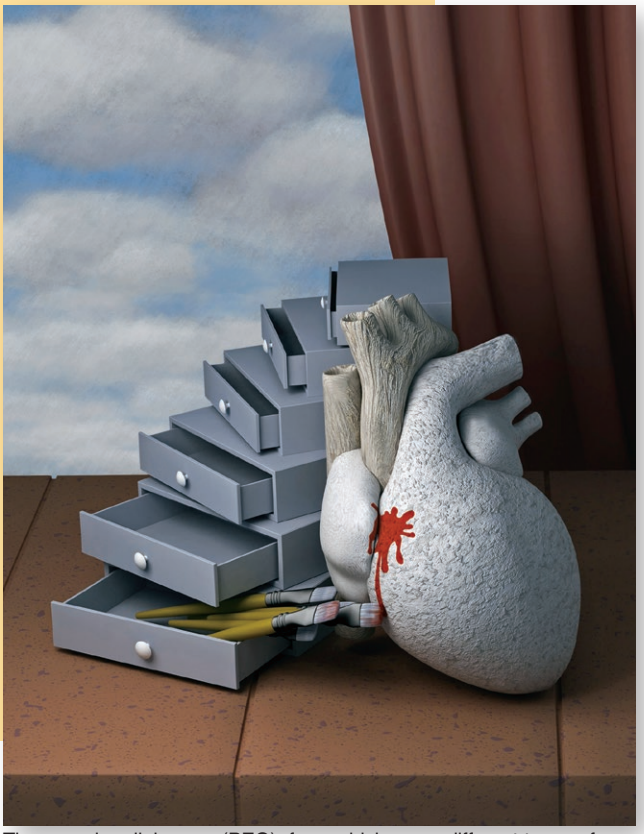
A Double Career That Spans Continents

Yang's colleagues saw what Guo could do, and that's how things took off at Penn. So far, she has designed more than 15 submitted journal covers, the logo for the Career Development Association at Penn, and three entries for the Philadelphia Science Festival Art Exhibit in 2011, among other projects.

But her double career, in fact, started before she began her doctoral work at Penn. While studying for an associate's degree in art in China, she transferred to a four-year college as a major in life sciences.

While she was there, a professor recruited her to illustrate a microbiology text book: "It was a perfect fit of my major and my talent."

Most of her work for the journal covers is designed on Photoshop. The most recent, for example, was for Penn biochemist Gideon Dreyfuss, Ph.D., for a cover on a recent paper in Cell for which he was senior author. Its title: "U1 snRNP Determines mRNA Length and Regulates Isoform Expression." The cover image depicts the molecular "struggle" between legions of U1 snRNP (small nuclear ribonucleoprotein), shown as knight-like defenders, protecting nascent pre-mRNA from the constant threat of cleavage and polyadenylation, represented by hordes of Vikings riding on the tail of RNA. The conceptual design was by Dreyfuss and the artwork by Guo, Chonghui Ma, and Zhaoming Guo.



The proepicardial organ (PEO), from which many different types of heart tissues are derived, is organized into genetically distinct subcompartments ("drawers"). The white model heart represents a developing heart in the process of being coated by PEO cells, which will gradually cover its surface and give rise to different heart tissues.

In this fanciful image of a circadian clock, the "Jack" from a deck of cards represents the JAK/STAT signaling pathway. The "Jack" holds a "sword" – a precursor microRNA in stem-loop shape.

Guo is nearly done with her Ph.D. work and is now writing papers based on that research.

When she feels the stress related to research and the publication grind, she has found that art is her way to relax. "It's a way to balance my life."

And, like Oppenheimer, she has come to appreciate the commonalities in the process of certain kinds of art and science: both start with teamwork, both fill in details along the way, and both explore different paths until a fuller, more finished form emerges. ●

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That's right, you did it. Your generosity turned *Making History* from a name into a campaign come true.

With a final total of $1.37 billion, Penn Medicine's biggest yet, the giving was historic. And with changes like the doubling of medical student aid, 40 new endowed professorships, and more than one million square feet of spectacular new research and care facilities, the impact will be felt for generations to come.

Thank you. Each gift contributes to the power of medicine to add compassion, inspiration, healing, and hope to life.

And as we approach the Perelman School's 250th anniversary in 2015, each gift strengthens our shared cause – to bring superior health care to our region, to remain a destination for the best students and faculty in America, and to make the breakthroughs that will bring better health to our world.

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The ideals of innovation, excellence, achievement, and public relevance are alive and well at the **Perelman School of Medicine**. They continue to inspire, and, with a historic naming gift, unprecedented student financial aid, and record-setting annual giving, alumni and friends are readying the school to lead in the 21st century.

Strong leadership will be paramount in the century ahead. Medicine, with its complexity, rapid change, immense relevance to our lives, and need for precious public resources, is front and center in today's struggle to define the public good.

President Amy Gutmann, Ray Perelman, and Dean J. Larry Jameson, M.D., Ph.D., are flanked by Perelman Scholars.

One key: providing the best doctors and freeing them from debt so they may pursue their ideals of service. Ray Perelman made his $225 million gift because he believes "the key is to get brilliant students into the system who will make brilliant doctors."

Campaign Chair Rosemary Mazanet, Ph.D. '81, M.D. '86, and Mrs. Barrie Jordan. Dr. Mazanet made the first pledge to the Jordan Challenge in part to support her friend and mentor, the late Henry A. Jordan, M.D. '62. G.M.E. '67.

Many participated in the innovative **John Morgan Scholars Program**, which matched gifts with funds provided by the Jordan family.

And longtime champions of scholarships and their liberating effects, Anne and Walter Gamble made several multi-million-dollar Campaign gifts. The family of **Gamble Scholars** followed suit: Every one of them contributed to a scholarship fund honoring the Gambles.

The Class of 1966 was one of the first to start a class scholarship fund.

Scholarship recipient Lucy Marcil

And the results are already being felt by students on campus today: Fourth-year Lucy Marcil writes, "Having financial aid during medical school truly makes a huge difference in my life. I will pursue a medical career caring for the underserved instead of worrying about my own personal finances."

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$225 million naming gift = Largest single gift to Penn and to name a medical school in the United States

Size of Smilow Center for Translational Research = **500,000 square feet**, making it the Perelman School's largest building

Gifts to the Abramson Cancer Center = **$216 Million**

Planned Giving = **10% of Campaign Total**

SOME!

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Walter Gamble, M.D. '57, congratulates Gamble Scholar David Chacko, M.B.A. '11, M.D. '11.

PROFESSORSHIP NAME	DEPT OR CENTER
The Robert C. Austrian Professorship	Perelman School of Medicine
The Basser Professorship in Oncology	Abramson Cancer Center
The Clyde F. Barker – William Maul Measey Professorship in Surgery	Surgery
The Helene Blum Assistant Professorship	Radiation Oncology
The Cali and Weldon Research Professorship in FOP	Orthopaedic Surgery
The Sidney D. Caplan Professorship in Bioethics	Medical Ethics and Health Policy
The Edward S. Cooper, M.D./Norman Roosevelt and Elizabeth Meriwether McLure Professorship	Medicine
The Craig and Elaine Dobbin/Nancy P. Blumenthal Professorship for Advanced Lung Disease	Medicine
The Founder's Associate Professorship in General Internal Medicine	Medicine
The Founder's Professorship in Urology	Surgery
The Gerd Muehllehner Professorship in Radiology	Radiology
The John H. Glick, M.D., Abramson Cancer Center Director's Professorship	Abramson Cancer Center
The Deenie Greitzer Gastrointestinal Medical Oncology Professorship	Abramson Cancer Center
The Paul R. Gross, M.D., Professorship for Director of Dermatology Education	Dermatology
The Guggenheim Family – Thomas W. Langfitt, M.D., Professorship	Neurosurgery
The Frank A. and Gwladys H. Elliott Chair in Neurology	Neurology at Pennsylvania Hospital
The Paul F. Harron Jr. Family Professorship	Medicine
The Paul F. Harron Jr. Professorship in Pulmonary Medicine	Medicine
The Leon Hess Professorship in Internal Medicine	Medicine
The F. M. Kirby Chair in Molecular Ophthalmology	Ophthalmology

PROFESSORSHIP NAME	DEPT OR CENTER
The G. Clayton Kyle, M.D., Professorship in Diabetes	Medicine
The Robert & Margarita Louis-Dreyfus Associate Professorship	Abramson Cancer Center
The Mariann T. and Robert J. MacDonald Professorship in Breast Cancer Care Excellence	Abramson Cancer Center
The Mariann and Robert MacDonald Women's Cancer Risk Evaluation Center Directorship	Abramson Cancer Center
The McLure Professorship in Psychiatry	Psychiatry
The Robert L. McNeil Jr. Professorship in Translational Medicine and Therapeutics	Institute for Translational Medicine and Therapeutics
The John Miclot Professorship of Medicine	Medicine
The John J. Mikuta, M.D., Professorship in Gynecological Oncology	Obstetrics and Gynecology
The Penn Medicine at Radnor Clinical Excellence Endowed Professorship	Medicine
The Ruth C. and Raymond G. Perelman Professorship in Internal Medicine	Medicine
The Rhoads-Harrington Professorship in Surgery	Surgery
The Henry Royster – William Maul Measey Professorship in Plastic and Reconstructive Surgery	Surgery
The Ernest F. Rosato – William Maul Measey Professorship in Surgical Education	Surgery
The Robert L. Sadoff Professorship in Forensic Psychiatry	Psychiatry
The Schaeffer Professor in Medicine	Medicine
The William Smilow Professorship	Medicine
The Albert J. Stunkard Professorship	Psychiatry
The Richard W. Vague Endowed Professorship in Immunotherapy	Abramson Cancer Center
The Ferdinand G. Weisbrod Professorship in Gastroenterology	Medicine
The Wilmott Family Professorship	Medicine

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Benjamin Franklin, the first donor to our hospitals, had a way of making history. Campaign donors followed his lead, establishing groundbreaking programs and facilities to the great benefit of Philadelphians today.

PATIENTS FIRST!

Spacious, light-filled, and welcoming, the **Perelman Center for Advanced Medicine** is a world-class outpatient care center right here in Philadelphia. Established with the naming gift of Ruth and Raymond Perelman and the founding gifts of 90 families, the Perelman Center delivers the comfort, convenience, and expertise families want when facing difficult disease.

Dear Dr. Parmacek,

The moment I stepped into the lobby of the Perelman Center, I felt the tension and fear start to leave me. . . . Every person I have been in contact with there has shown tremendous kindness, understanding, and confidence.

My three little grandchildren know all about my new doctor who figured out what is wrong with Gram and is going to help her live a long time to watch them grow. They love hearing about the cool tests and wonderful new ways he helps tons of people.

I look forward to my future visits and if you ever see Mr. Perelman, please remember to give him my deepest thanks for making this possible for me and everyone who steps into the Perelman Center.

Sincerely,

Patricia Reitano

CANCER THERAPY FOR AN ACTIVE LIFE

"Welcome Aboard, Mr. Proton," were Ralph Roberts's words at the dedication of the **Roberts Proton Therapy Center**. Since then, the easier-to-tolerate radiation therapy that is the hallmark of the Center has allowed world travelers, fly fishing and golf devotees, skydivers, parents, and students to continue with their busy lives. At least two patients truly are on board with the Center: one man took the bus, while another rode his bike to each therapy session.

"The machine at the Roberts Proton Therapy Center is amazing, but it is the people behind the machine that made all the difference in my cancer treatment and recovery. After my last treatment I felt a loss because I would no longer see these

Mr. McKee and his son, Frank McKee Jr., ring the ship's bell they gave to the Center for patients to ring when they complete their treatment.

people every week. They made me feel like I was a part of a family, which was critical to my recovery," said Frank McKee, an early patient of the Center. Mr. McKee is a founder of the Roberts Proton Therapy Alumni Group, volunteers who came together to support, educate, and cheer one another and those entering proton radiation therapy onward.

PHILADELPHIA'S FIRST ADULT TRANSPLANT HOUSE

is a true community effort. More than 1,000 donors – the friends and families of transplant patients, construction and other vendors, and Penn Transplant Institute faculty and staff – contributed to the Clyde F. Barker Penn Transplant House.

PENN RESEARCH

WHERE CURES BEGIN

A young girl who nearly died from leukemia – and today is leading a normal life. Grandparents whose lives have been extended by innovative new cardiovascular procedures. Children with better eyesight restored.

We are all proud, humbled, and happy to spread the news when our physicians achieve impossible dreams like these. Research at Penn brought these outcomes to fruition over the Campaign years. Each took years to accomplish, and Campaign

Emily Whitehead and her parents came to the meeting of the Abramson Cancer Center Director's Leadership Council to thank Penn for her return to health. Because of a clinical trial for an immunotherapy developed by Carl June and his team, Emily's nearly fatal leukemia is now in remission.

giving recognized these landmark accomplishments while laying the groundwork and expressing hope for breakthroughs to come.

With $731 million in gifts, biomedical research is the most strongly supported campaign priority. Whether their gifts established a whole new Center or helped the annual fund climb a notch higher, families gave to Penn Medicine to end a wide range of diseases and create a legacy of better health for the next generation.

Joel (left) and Bill Smilow established the 500,000-square-foot Smilow Center for Translational Research. "We are delighted to make this significant contribution to advancing health care in our nation and around the world," said Joel.

The Gray and Basser families joined Penn leadership to celebrate the establishment of the Basser Center.

Former Abramson Cancer Center Directors John H. Glick, M.D., and Richard "Buz" Cooper, M.D., (at each end) and Madlyn and Leonard Abramson welcomed current director Chi V. Dang, M.D., Ph.D., in 2011.

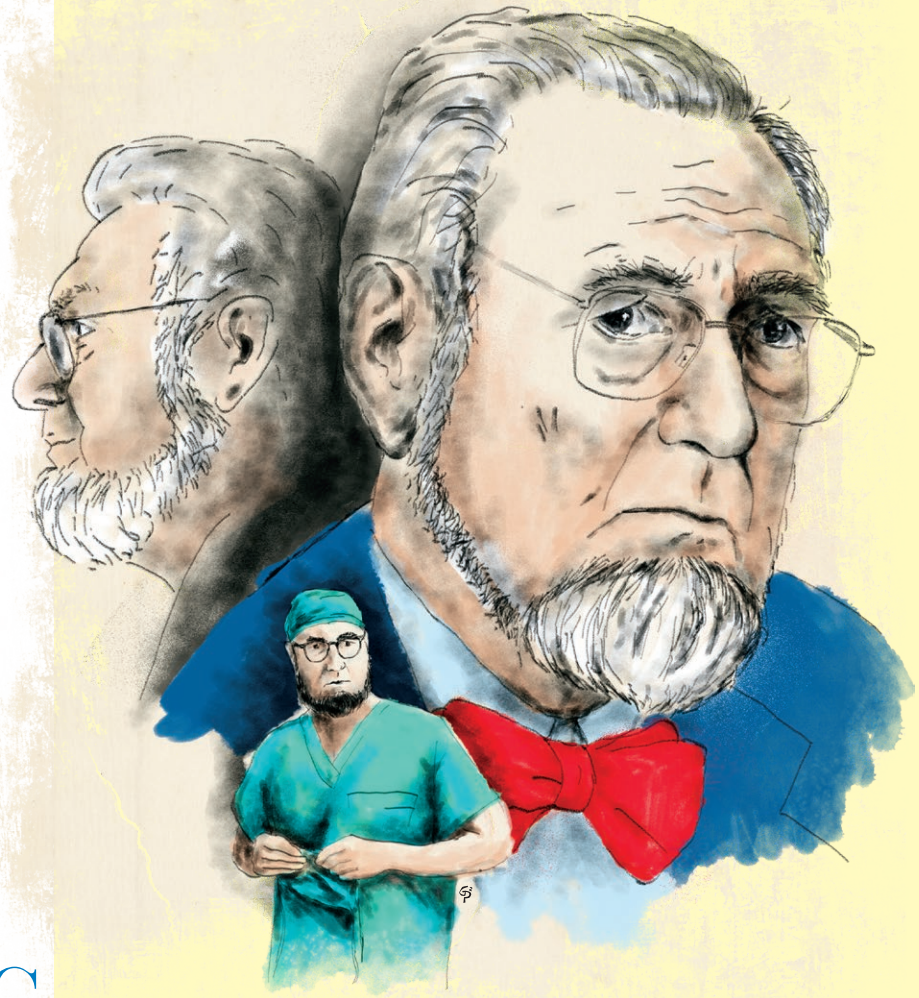
EXCEPTIONAL.

The **Abramson Cancer Center** is rated #1 in the region, and in 2010 it received the NCI's top rating of "exceptional." More than 30,000 donors gave to support this focal point of cancer care and research innovation.

MAJOR PROGRAMS ESTABLISHED DURING THE *MAKING HISTORY* CAMPAIGN

Basser Research Center for BRCA
Jordan Center for Gynecological Cancer
MacDonald Women's Cancer Risk Evaluation Center
Neuroscience of Behavior Initiative
Penn Center for Orphan Disease Research and Therapy

C. Everett Koop: A Surgeon, an Educator, and a Man Who Spoke His Mind



C. Everett Koop, M.D., G.M.E. '47, the former Surgeon General who died on February 25 at the age of 96, was of course a national figure. *The New York Times* noted that he "was widely regarded as the most influential surgeon general in American history" (25 February 2013). But Koop also had a long and very fruitful connection to the University of Pennsylvania and the City of Philadelphia. Indeed, as *The Philadelphia Inquirer* put it in an editorial after his death, "Koop grew up in Brooklyn, N.Y., but Philadelphians considered him one of their own."

After earning his M.D. degree from Cornell Medical College in 1941, Koop served an internship at Pennsylvania Hospital and did additional training at Penn's School of Medicine and Boston Children's Hospital. He completed his training at Penn's old Graduate School of Medicine, from which he received a Doctor of Science (Medicine) degree in 1947. He was named professor of pediatric surgery at Penn in 1959 and professor of pediatrics in 1976. Even before that, however, he had greatly impressed I. S. Ravdin, M.D. 1918, then Penn's chair of surgery, who offered him a job as surgeon-in-chief of the Children's Hospital of Philadelphia in 1948. As *The New York Times* stated, it was "a rare offer for someone so young." He served in that capacity until he left academe in 1981 to become Surgeon General.

Koop was a pioneer in the development of newborn surgery, known for his innovations and for perfecting its new techniques. Under his guidance, Children's Hospital created the first neonatal surgical intensive-care unit in the United States. He was also the first surgeon to separate Siamese twins joined at the heart.

As a faculty member of Penn's medical school, Koop was also one of the prime movers in the creation of the *Journal of Pediatric Surgery*. He was its founding editor, a position he retained for 11 years.

On a different note, for about 25 years now, many students of Penn's School of Medicine have been very active in volunteering at the University City Hospitality Coalition clinic and the United Community Clinics. There was similar activity in the late 1940s, when Penn medical students established clinics for needy Philadelphians, based at neighborhood missions. At first, the participating students were all members of the Christian Medi-

cal Society at Penn, but that eventually changed. Koop, then a young assistant professor of surgery, was one of the people who joined the students at the clinics, and he became their graduate director.

Among his many honors, Koop was a member of two historic Philadelphia organizations, the American Philosophical Society and the College of Physicians of Philadelphia, which maintains the Koop Education Center for schoolchildren. He received an honorary doctorate from the University of Pennsylvania in 1990, during its 250th anniversary celebrations. In 1994, Koop was presented with the Distinguished Graduate Award, the highest honor the Perelman School of Medicine bestows on alumni, in recognition of his outstanding accomplishments in pediatric surgery and his administration of the Office of the Surgeon General. Koop's other honors included the Presidential Medal of Freedom and France's Medal of the Legion of Honor, as well as induction into the Royal College of Surgeons of England.

As J. Larry Jameson, M.D., Ph.D., dean of the Perelman School of Medicine and executive vice president of the University of Pennsylvania for the Health System, put it: "Our School, our city, and our nation have lost one of our leading citizens."

> As a professor of pediatric surgery and of pediatrics in Penn's medical school, Koop was also one of the prime movers in the creation of the *Journal of Pediatric Surgery*. He was its founding editor, a position he retained for 11 years.

Koop was also known for his strong views. Two years before he was appointed Surgeon General by President Reagan, he was one of the authors of *Whatever Happened to the Human Race?*, which was forcefully against abortion. Such advocacy disturbed liberals. But Koop then surprised people on both sides of the political aisle when, as Surgeon General, he refused to issue a report declaring that abortion was harmful to women. In his memoir, *Koop: The Memoirs of America's Family Doctor* (1992), excerpted at the time in *Penn Medicine*, he argued that the scientific data was not there to support such a view. "Abortion was more a moral issue than a medical issue." Unlike the data about AIDS, he wrote, "The question of abortion and its health effects on the mother could not draw on the same kind of data and interpretation."

In addition to confounding expectations on the medical aspects of abortion, Koop also upset many early conservative supporters from tobacco-growing states when he began to campaign vigorously against smoking. Included in that campaign was a report stating that secondhand smoke had been conclusively proven to cause cancer. As he put it in *Koop*, describing the uniform he wore as surgeon general: "Over the years I accumulated a few decorations for this and for that, and when someone asked me what my ribbons were for, I would always reply, 'The top row is for what the liberals did to me; the bottom row is for what the conservatives did to me.'" ●

A Return to Penn

In 1996, C. Everett Koop, M.D., returned to the Penn campus to deliver the Robert G. Ravdin Memorial Lecture, sponsored by the Department of Surgery. Although the health-care marketplace has changed to some extent in the intervening years, Koop's use of history and his championing of the doctor-patient relationship – "the heart and soul of medicine" – come through in his distinctive voice. What follows is an edited version of his remarks.

Patients tell me that they don't trust doctors the way they did in the past, and they find doctors to be impersonal, aloof, difficult to understand, and always overly busy. Doctors tell me that their patients are sullen or aggressive, and that the shadow of litigation frequently darkens a doctor-patient encounter, making the doctor afraid even of the person he seeks most to help at that particular time.

For most of medical history, diseases were rarely understood, pain and death could rarely be averted, and the most dramatic therapies of choice – bleeding and cupping, purging and blistering – were embraced by doctor and patient alike not out of any empirical evidence that they were beneficial, but out of the conviction that the doctor had to do *something* for his patient. Now this was not an era of idyllic patient-doctor relationships, because usually that *something* was as painful and debilitating a procedure as it was ineffective.

In the first part of the nineteenth century, the doctor-patient relationship entered a new phase. In this era, many people concluded that doctors had very little in their black bags that could actually *cure* people and that ordinary people could do their own doctoring as well as some physicians. So from the eastern seaboard to the western frontier, alternative medical sects began to flourish for profit; fly-by-night medical schools sprang up; purveyors of miracle medicines fleeced the public; and regular doctors were forced to out-hustle each other in a medical marketplace.

In the late 19th century and early 20th century, the efficacy of medicine and the quality of the doctor-patient relationship took a dramatic upswing. Medical milestones – such as anesthesia, antisepsis, antitoxins, antibiotics – at last meant that doctors could really do something to cure disease, to alleviate suffering, and, indeed, to prolong life. And patients responded by placing unprecedented trust in their doctors. And society then responded by affording the medical profession the honor and the authority and the wealth and the power to which it became accustomed in the middle third of this century.

But then came the breakdown of the so-called "payer-provider pact." In its heyday, from World War II until [the 1980s] or so, the payer-provider pact meant that, in most cases, insurance companies willingly paid whatever physicians charged for whatever it was that they did. While it lasted, it meant for most Americans, for the first time in history, economic considerations were usually removed from the patient-doctor relationship. Then, as health-care costs soared out of sight in the 1980s, driven up by a variety of factors – expensive technology, malpractice expenses, the need to practice defensive medicine, physicians' fees, an aging population, and so on – the payer-provider pact came undone. The people who paid the most health-care insurance – that is, companies, businesses, and taxpayers – said, "Enough is enough." And suddenly, economic issues once again began to play a major role in doctor-patient relationships.

These economic issues lie behind the managed-care movement. In its broadest sense, managed care means that no longer will doctors be able to do whatever they want to do and to charge whatever they want to for doing it. Economic factors began to alter the doctor-patient relationship as never before, as more people – insurance clerks, business CEOs, company controllers, and a variety of bean-counters – in their combined efforts to hold down costs, crowded into the doctor's office to intrude into a relationship that, until recently, had been just between a single patient and a single physician.

Now, while I am a believer in and a beneficiary of the free-enterprise American economy, I have some real reservations about the ability of market forces alone to do what is best for the health of the American people. I am deeply concerned about the millions of Americans who live in poverty on the very fringes on this otherwise affluent society, our fellow citizens for whom market-driven health care will offer less and less.

> "I am deeply concerned about the millions of Americans who live in poverty on the very fringes on this otherwise affluent society, our fellow citizens for whom market-driven health care will offer less and less."

I don't want my remarks to be interpreted as a diatribe against the negative effect of managed care on the doctor-patient relationship. In some ways, managed care *could* make that relationship even better, as some recent studies on Medicaid patients who were shifted to managed care have shown – higher patient approval with managed care than in the previous system. And recently, some managed-care groups have taken seriously their obligation to the community, even those who were not their clients.

But it seems clear that the demands for economic efficiency will mean that doctors will be forced to spend less and less time with each patient; and that will have a corrosive effect on the doctor-patient relationship – particularly at a time when medicine is much more complicated than it was, and when patients seem to want to know more and more.

The most disturbing impact of managed care on the doctor-patient relationship is the way in which managed care can create a financial incentive for the physician to withhold necessary medical treatment from the patient. This could create a very dangerous conflict of interest between the doctor and his patient and could threaten to eradicate what trust remains between physician and his patient.

But we also need a revitalization of physician professionalism and a refined understanding of patients' rights as well as their responsibilities. I think many of the problems that managed care has presented to medicine might have been avoided to some degree if physicians had not let their sense of professionalism languish. Members of a profession are expected to police themselves, but we must admit that medicine – along with some other professions, particularly law – has too often coddled the bad apples instead of removing them. I imagine that very few Americans today would say that physicians embody an ethic higher than that of society at large, as once was the case.

Finally, members of a profession are expected to place the interests of those they serve – patients, clients, students, etc. – above their *own* interests. And managed care will either bury this hallowed hallmark of the medical profession, or this commitment to professionalism will correct many of the problems of managed care. And along with a refurbished commitment to medical professionalism, we also need a revitalized patient-rights movement which can draw the best from managed care. ■

Progress Notes

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Philadelphia, PA 19104-3309

'50s

William E. Bunney Jr., M.D. '56, the Distinguished Professor of Psychiatry & Human Behavior at the University of California at Irvine, was a recipient of the 2012 Pioneers in Psychopharmacology Award from the International College of Neuropsychopharmacology. According to the college, the contributions of the honorees "must be internationally recognized as significant to the growth of the field." Bunney, who also holds the Della Martin Chair of Psychiatry, is a neuroscientist focused on discovering the genes that cause major depressive disorder, schizophrenia, and bipolar disorder. Bunney was also one of the two recipients of the 2011 Rhoda and Bernard Sarnat International Prize in Mental Health, presented by the Institute of Medicine. Bunney and Ellen Frank of the University of Pittsburgh School of Medicine, were honored for their complementary achievements in enhancing treatment and understanding of mood disorders. Bunney is the author of more than 390 scientific publications and the editor of seven books.

'60s

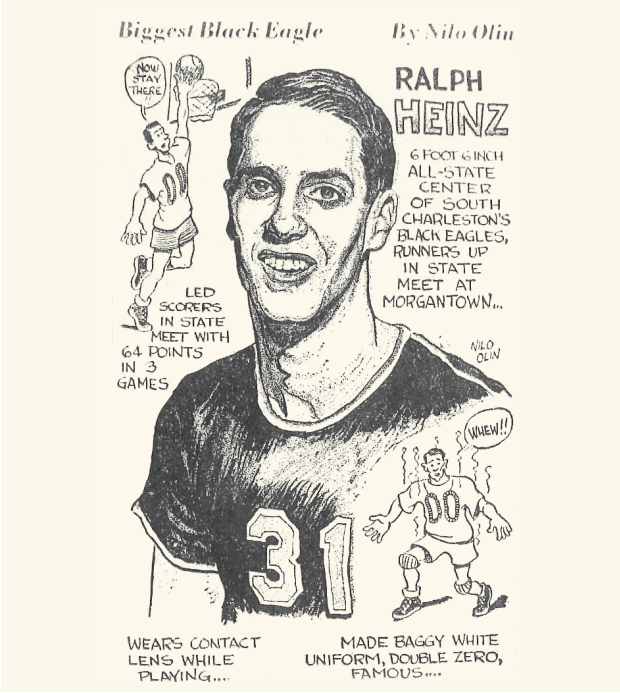
Stanley J. Dudrick, M.D. '61, G.M.E. '67, has joined American Outcomes Management, L.P., a national company owned and operated by physicians that provides home IV therapy. He is medical director for nutritional services. Dudrick is recognized as one of the "fathers" of total parenteral nutrition (TPN), along with the late Jonathan E. Rhoads, M.D., former chairman of surgery at the University of Pennsylvania. Dudrick's groundbreaking work in nutrition while at Penn established the research basis for the use of TPN in the clinical setting. He was one of the founders of the American Society for Parenteral and Enteral Nutrition and served as its first president. He is also a recipient of the Distinguished Graduate Award, the highest honor bestowed by the Perelman School of Medicine.

F. Joseph Hallal, M.D. '66, was named senior manager by ECG Management Consultants, Inc., a health-care management consulting firm. Hallal has more than 40 years of experience in patient care and leadership in management, patient safety, and quality issues. Most recently in his career, he was a consultant for the Center for Medicare and Medicaid Innovation (CMMI), the branch of CMS that is developing and piloting new programs, as mandated by the Affordable Care Act. Before that, he was at Inova Fairfax Hospital, where he had served as director of the cardiac catheterization laboratory at, president of the medical staff, and chief medical officer.

Marvin "Spike" J. Lipschutz, M.D. '68, has become vice president for medical services and chief medical officer of Greenwich Hospital, a member of the Yale New Haven Health System. He retains his prior duties as chief quality officer. Before coming to the hospital in 2007, he served as senior vice president of medical affairs at South Shore Hospital in Massachusetts.

'70s

Robert P. Lisak, M.D., G.M.E. '72, received the 2013 Gold Medal for Achievements in Medical Research from the Alumni Association of Columbia University's College of Physicians and Surgeons. He has been a national leader in basic, clinical, and translational research related to multiple sclerosis, myasthenia gravis, immune neuropathies, and neurologic complications of systemic autoimmune diseases. A faculty member at the University of Pennsylvania for 15 years, he was chairman of neurology at Wayne State University School of Medicine and neurologist-in-chief at the Detroit Medical Center until 2011. He was editor of the *Journal of the Neurological Sciences* from 1998 to 2012.



E. Ralph Heinz, M.D. '55, emeritus professor of radiology at Duke University, was interviewed last year in the *American Journal of Neuroradiology*. A former vice president of the American Society of Neuroradiology, he received its Gold Medal Award in 2004. In his career, he has been chief of neuroradiology at Yale University, chair of radiology at the University of Pittsburgh (where the department had two of the first five computed tomography units in the country at that time), and chief of neuroradiology at Duke, where there is a named lectureship in his honor.

After his residency, Heinz was also a fellow in radiology with Juan Taveras, M.D. '49, a recipient of the Perelman School of Medicine's Distinguished Graduate Award, who was considered one of dominant forces in establishing and advancing the specialty of neuroradiology. Here Heinz describes a "normal day" with Taveras: "We started a 8 a.m. with a schedule that included 3-6 diagnostic angiograms, 4 myelograms, and 3 pneumoencephalograms. . . . Like clockwork every day, Dr. Taveras would come down to the reading room at 3 p.m., dressed very formally in a long white coat. He would spend about 3 hours with us interpreting the studies. He was simply fantastic at it. He would pay $5 to anyone who found an abnormality he missed and 50 cents for every finding that he had seen but was mentioned by someone before him. It was just a standing joke, he would have paid, but he never had to!"

When asked what he would tell someone who is considering a career in his field, Heinz noted the new importance of nanotechnology and functional imaging. "We are at the threshold of the most exciting times for neuroradiology. The purpose of all this is to bring a multidisciplinary approach to brain function."

But the interview in the *Journal* also revealed another side of Heinz – the athlete. He started playing basketball in high school and went to college on a basketball scholarship. In fact, even when he started medical school, he continued playing basketball with a semiprofessional team. "I managed to do both for a while, and then medicine took over my life and I was forced to give up basketball." (The drawing shows him at the time he led his high-school team to the state championship game in West Virginia. Along the way, he scored 35 points in one game and led all scorers in the state meet.)

'80s

Amanda Sue Carlisle, M.D. '81, Ph.D., was named vice dean of San Francisco General Hospital & Trauma Center in July 2012. As associate dean and vice dean, she has advocated on behalf of the faculty at SFGH, helped steer it through changes in leadership, established collegial working relationships with the Department of Health administration, and led the participation of the University of California at San Francisco in the rebuilding of San Francisco General Hospital. Carlisle is a recipient of the Stuart C. Cullen, M.D., Award for Clinical Excellence (1990), the Faculty Clinical Excellence Award (1993), and the 2012 Chancellor's Award for the Advancement of Women. She is a former chief of anesthesia at the hospital.

William J. Henry, M.D. '83, G.M.E. '89, an otolaryngologist, has joined the staff of Aria Health, the largest health-care provider in Northeast Philadelphia and Bucks County. He is a member of the American Academy of Otolaryngology – Head and Neck Surgery and the American Academy of Facial Plastic and Reconstructive Surgery.

Robert P. Lanza, M.D. '83, chief scientific officer at Advanced Cell Technology, Inc., was appointed editor-in-chief of *BioResearch Open Access*. The peer-reviewed journal offers rapid publication on scientific topics including molecular and cellular biology, stem cells, gene therapy, biochemistry, microbiology, and neuroscience.

Anjan K. Chatterjee, M.D. '85, was named to the board of the Associated Services for the Blind and Visually Impaired. He is a professor of neurology at the School of Medicine at the University of Pennsylvania and a researcher at the Center for Cognitive Neuroscience.

Debra A. Schwinn, M.D., G.M.E. '86, was named dean of the University of Iowa Roy J. and Lucille A. Carver College of Medicine. Schwinn had been as professor and chair of the Department of Anesthesiology and Pain Medicine at the University of Washington in Seattle and had held the Allan J. Treuer Endowed Professorship there. She is a nationally known investigator in molecular pharmacology with active funding from the National Institutes of Health and received the 2007 Excellence in Research Award from the American Society of Anesthesiologists.

David A. Mankoff, M.D. '88, Ph.D., has joined the nuclear medicine division of Penn's Department of Radiology as chief of nuclear medicine and clinical molecular imaging. Most recently, he was an attending physician at the Seattle Cancer Care Alliance. Mankoff has focused much of his research on developing and translating novel molecular imaging approaches to characterize cancer and its response to therapy. He has been listed in Best Doctors in America and has received the Distinguished Scientist Award from the Western Regional Society of Nuclear Medicine. His doctoral degree is in bioengineering from the University of Pennsylvania.

'90s

Dana C. Covey, M.D., G.M.E. '90, was elected to the board of councilors of the American Academy of Orthopaedic Surgeons. He is a member of the teaching faculty at Naval Medical Center, San Diego, and a clinical professor orthopaedic surgery at the University of California at San Diego. He has twice deployed to Iraq with the Marines and, from 2010 to 2011, was officer-in-charge of Marine Corps forward surgical teams in to Afghanistan. He is a diplomate and oral examiner of the American Board of Orthopaedic Surgery and a member of the American Orthopaedic Association. His honors include the Colonel Brian Allgood Memorial Award for Excellence in Military Orthopaedic Leadership, the Chairman of the Joint Chiefs of Staff Award for Excellence in Military Medicine, and the Sir Henry Wellcome Medal and Prize for outstanding military medical research. He has also received the Bronze Star Medal (U.S.M.C.) and the Legion of Merit (Navy).

James S. Kuo, M.D. '90, M.B.A., was appointed chairman and chief executive officer of BioSavita, Inc., which seeks to bring new antibody medicines to patients in partnership with biopharmaceutical companies. Kuo has more than 20 years of experience as a venture capitalist, pharmaceutical business development executive, and senior manager of private and publicly traded biotech companies. The founder and former chief executive officer of Discovery Laboratories, Kuo is currently chairman of the board at MSK Pharma, a pharmaceutical company specializing in pain and musculoskeletal diseases, of and Monarch Labs, a maker of medical devices for wound care.

Gerald M. Lemole Jr., M.D. '95, was elected to a two-year term as chief of staff at The University of Arizona Medical Center and serves as chief administrative officer for the physicians who practice at the university campus. He also chairs the hospital's medical executive committee. A professor of surgery and chief of the division of neurosurgery at the UA Department of Surgery, Lemole is an expert in skull-base surgery.

Tara D. Butler, M.D. '98, was appointed to the board of directors at PathoGenetix, the developer of genome sequence scanning technology. She currently serves as investment director at Ascension Health Ventures, a faith-based investment group that funds companies that offer products related to health care. She has held positions in business development at Medtronic and in finance at Honeywell. She also serves on the board of Isto Technologies, an orthobiologics company, and Neurolutions, Inc., which seeks to harness the brain's electrical signals for communication and control systems for people with severe motor disabilities.

OBITUARIES

'30s

George Van Buren, M.D. '39, Akron, Ohio; July 27, 2012. He served four years as a medical officer in the U.S. Army during World War II. He was a pioneer in providing equal access to high-quality medical care to all persons. In 1941, he was honored by the American Medical Association and the American College of Orthopedic Surgeons for his successful breakthrough in developing a pain-free, non-surgical treatment of osteomyelitis.

'40s

Thomas M. Baldwin Sr., M.D., G.M. '40, Friendship Ridge, Pa.; May 2, 2012. He started his practice in Beaver Falls in 1942 and retired in 1984. He was a former president of the medical staffs at the New Brighton Hospital and Providence Hospital in Beaver Falls. From 1952 through 1960, he was editor of the Beaver County Medical Society Bulletin. He was a diplomat of the American Board of Otolaryngology.

Paul DeCamp, M.D. '40, New Orleans; August 5, 2012. He was a cardiovascular surgeon at Ochsner Clinic for 40 years. He was the assistant chief of surgery and was a member of the team that achieved the first successful kidney transplants on an adult and on a child. He was on the Alton Ochsner Medical Foundation Board of Trustees and its executive committee.

George W. Corbin Jr., M.D. '43, Raleigh, N.C.; June 21, 2012. He was a WWII veteran of the U.S. Army and a Korean War veteran of the U.S. Air Force. He practiced medicine in the Wake Forest area for more than 40 years before retiring in 1985.

Ruth Breitwieser Dunning, M.D. '43, G.M.E. '47, Allentown, Pa.; August 31, 2012. She worked as a physician at Wellesley College's student health services for 16 years. She then became a staff physician at the University of Pennsylvania's student health service. She was also a member of the auxiliary staff of Pocono Hospital, a physician with the State of Pennsylvania's Well Baby Clinic in Stroudsburg, and a school physician for the Pleasant Valley School District.

Ralph E. Teitgen, M.D. '44, Fox Point, Wis., a retired ophthalmologist; November 21, 2010. He served in the U.S. Army and achieved the rank of captain. He earned a fellowship in ophthalmology from the Mayo Clinic in Rochester, Minn., and received his M.S. degree in ophthalmology

from the University of Minnesota. He had been had been an associate clinical professor of ophthalmology at the Medical College of Wisconsin and served on the board of directors of Prevent Blindness Wisconsin.

Willard E. Dotter, M.D. '45, Weston, MA; May 28, 2012. After serving in the Navy from 1945 to 1948, he joined the orthopaedic department of the Robert Packer Hospital-Guthrie Clinic. Later, he was with the Great Falls Clinic in Great Falls, Montana, and the Lahey Clinic Orthopedic staff until he retired in 1987.

Mary L. Hansen, M.D.'45, Bryn Mawr, Pa.; June 9, 2012. In the 1940s, she was a staff psychiatrist at Philadelphia Psychiatric Hospital and Philadelphia State Hospital. In the 1960s she joined the staff at Haverford State, where she was a staff psychiatrist until she retired in 1989. She was a founding member of the Pennsylvania Association of State Mental Hospital Physicians, where she served as secretary.

James M. Keiter, M.D.'46, Harrisburg, Pa.; September 4, 2012. He served in the military as a medical officer at Fort Leavenworth, Kansas, until his discharge in 1949 with the rank of captain. He spent the next 17 years practicing family medicine in Campbelltown, Pa. He worked as an emergency-room physician in a group medical practice that pioneered emergency-room services at the Good Samaritan Hospital in Lebanon until his retirement in 1987. During this period, he served as medical coordinator of the EMT training program in Lebanon County and as a preceptor in the M.S. Hershey Medical Center College of Medicine. He was a former president of the Lebanon County Medical Society and a former member of the board of the Lebanon County Mental Health & Mental Retardation.

James A. Dull, M.D. '48, G.M. '56, Greensburg, Pa.; July 30, 2012. He served on the medical staff at Westmoreland Hospital and Jeannette District Memorial Hospital for 35 years. He had been president of Westmoreland Hospital Association.

William A. Pratt, M.D., G.M. '49, Rutland, Vt.; April 5, 2008. He served as a captain in the U.S. Army Medical Corps. He opened his private practice in internal medicine in Rutland in 1949, and for approximately the next twenty years, he was the only board-certified internist in the county. As a member of the Rutland Regional Medical Center from 1949 to 1991, he served terms as chief of medicine and president of the hospital staff. Sub-specializing in cardiovascular disease, he founded the Associates in Internal Medicine in 1971. He was an instructor in clinical medicine at the University of Vermont's College of Medicine. He was also co-founder and president of the Vermont State Heart Association. Pratt was also former president of the American Society of Internal Medicine and a fellow of the American College of Physicians. He also served on the board of Blue Cross/Blue Shield of New Hampshire-Vermont.

'50s

Margaret A. Milliken, M.D., G.M. '52, Chevy Chase, Md., August 11, 2011. An internist, she earned her M.D. degree at the Medical College of Pennsylvania. She had been a medical officer for the Food and Drug Administration.

Ross S. McConnell, M.D. '52, Bromley, London, a specialist in occupational medicine; January 10, 2012.

Ellis P. Singer, M.D. '53, Westfield, N.J., a retired physician and pulmonary specialist; June 6, 2012. He served for two years in the U.S. Air Force. He was president of the New Jersey Chapter of the American College of Chest Physicians and had been clinical professor of medicine at the University of Medicine and Dentistry of New Jersey.

Lee H. Shields, M.D. '54, G.M.E. '60, Tampa Bay, Fla., retired cardiologist and internist; September 23, 2012. He served on active duty in the U.S. Navy for two years, including fifteen months aboard the U.S.S. Oglethorpe, during the Suez Crisis. He served in the Ready Reserve (USN) for another 11 years, retiring as a lieutenant commander. He was clinical associate professor of medicine at Penn State College of Medicine and serves as president of the South Central Pennsylvania Heart Association and as president of the Pennsylvania Heart Association. He was a fellow of the American College of Physicians, the American College of Cardiology, and the College of Chest Physicians. In 1977, he became president of the medical and dental staff of Polyclinic Clinic Hospital in Harrisburg, Pa.

Fred S. Winter, M.D., G.M. '54, Pottstown, Pa., a retired radiologist; September 23, 2012. As a member of the Navy Medical Corps, he served in both World War II and the Korean conflict. While a research fellow at the Cardiovascular Institute of Hahnemann Medical College and Hospital, he did pioneering work in developing a technique for coronary arteriography. In 1958, he received the Gold Medal from the American Roentgen Ray Society for his success in this field. Winter volunteered with CARE-MEDICO to train radiology residents in Afghanistan and helped McCormick Hospital in Chiangmai, Thailand, to improve its radiology department. A fellow of the American College of Radiology, he was an associate of radiology on staff at Pottstown Memorial Medical Center for 25 years. In 1994, he was honored by the Pennsylvania Medical Society and the Montgomery County Medical Society for his 50 years of service in medicine.

Jerrold G. Grofe, M.D. '55, Philadelphia; April 27, 2012. He joined the Army Air Corps in 1945 and served two years in Germany just after the close of World War II. He joined the faculty of the University of Pennsylvania as a staff psychiatrist before opening a private psychiatric practice. He returned to Penn in the early 1970s, then moved his office to Paoli in 1981. A former president of the Philadelphia Psychiatric Society, he was also a member of the Clinical Outpatient Mental Health Center in Easton.

George V. Hamrick, M.D., G.M. '55, Charleston, W. Va.; May 24, 2012. He served in the U.S. Army 1943-45 and 1951-53, attaining the rank of captain. A graduate of the University of Maryland School of Medicine, he began as a general practitioner before becoming an ophthalmologist. After moving to Charleston in 1958, he maintained an ophthalmology practice until retiring in 1988. He had been president of the West Virginia Academy of Ophthalmology and of the Kanawha Medical Society.

Stephen A. Ockner, M.D. '55, Cleveland, retired chair of general internal medicine at the Cleveland Clinic; April 17, 2012. After his medical training, he was assigned to Lockbourne Air Force Base (Strategic Air Command), and then to RAF Burderop Park and RAF Lakenheath (Tactical Air Command). His subspecialty training was at Peter Bent Brigham Hospital, following which he served his last duty station at Scott Air Force Base (Military Airlift Command). He served as chief of medicine and vice president of the Society of Air Force Internists and was involved in planning the medical care for returning Vietnam War POWs. He was awarded the Air Force Commendation Medal and the Legion of Merit. In 1975, he began his career at the Cleveland Clinic Department of Internal Medicine, where he eventually became director of the Internal Medicine Residency Program and chairman of the Geriatric Task Force.

Jay C. Alameda, M.D., G.M. '56, Peoria Heights, Ill., a retired orthopaedic surgeon; March 12, 2012. He enlisted in the U.S. Army and served as a captain within the orthopaedic department during the Korean War at the U.S. Army Hospital in Stuttgardt, Germany. He served on the staffs at OSF Saint Francis Medical Center, Methodist Medical Center, and Proctor Hospital and had a private practice in Peoria. The orthopaedic consultant at Easter Seal Orthopedic Clinic in Ottawa, Ill., for 32 years, he also performed the first total hip and total knee replacement surgeries in Peoria.

Charles A. Heisterkamp III, M.D. '58, Lancaster, Pa.; August 18, 2012. A longtime member of the U.S. Army Medical Corps, he commanded the Surgical Research Team of the Walter Reed Army Institute of Research, at a mobile surgical and research hospital during the Vietnam War, and later established and directed the Biomedical Engineering Program in the Research and Development Com-

mand of the U.S. Surgeon-General, where he assisted in evolving national trauma treatment protocols. He served as Commander of the 103rd Medical Battalion of the 28th Infantry Division, headquartered at Stahr Armory. He was a general and vascular surgeon, as well as a consultant in biomedical engineering and the use of computers in medicine. He also had a private medical practice. He was a pioneer in the use of computers in medical offices and worked to customize software for doctors' use. He introduced the first computerized doctor's office in Lancaster and his advocacy of the use of computers in medicine led the Australian and Canadian governments to consult with him and ask him to lecture at Medical Society meetings. A fellow of the American College of Surgeons, he was the first chairman of the Emergency Medical Council in Lancaster County and directed the training of more than 300 ambulance personnel. Heisterkamp also served as medical commander of the Lancaster County Civil Defense during the Three Mile Island crisis. He was instrumental in building the first ambulatory surgical center in Lancaster. He published extensively in the fields of surgical techniques, bioengineering, ambulatory surgery, and computers and medical office applications.

Richard H. Norton, M.D. '58, Virginia Beach, Va., a retired anesthesiologist and former head of anesthesia at Portsmouth Naval Hospital; November 20, 2011.

Jerry L. Doggett, M.D., G.M.E. '59, Houston; May 3, 2012. He served in the U.S. Army 1961-1963. He had been assistant chief of surgery at St. Luke's Hospital and served for many years as chairman of surgery at Kelsey Seybold Clinic.

Jamshid Hamed, M.D., G.M. '59, Towson, Md., a retired rheumatologist at the Greater Baltimore Medical Center; November 8, 2011.

'60s

June D. Unger, M.D., G.M.'60, Scottsdale, Ariz., a radiologist; March 19, 2012. From 1962 to 1985, she worked at the Veterans Administration Hospital in Milwaukee and was associate professor at the Medical College of Wisconsin. She then joined the University of Wisconsin in Madison, where she was a professor of radiology until 1995. Unger was a fellow of the American College of Radiology and had been president of the Milwaukee Roentgen Ray Society and of the Wisconsin Radiologic Society.

Hernando Trujillo, M.D., G.M. '64, Levittown, Pa.; May 24, 2012. He served as medical director at the Rohm and Hass Company from 1968 to 1978. As a surgeon, he was elected president of the medical staff at Lower Bucks Hospital three times and also served on the staff at Saint Mary Medical Center. He was honored by the Pennsylvania Medical Society and the American Medical Student Association in recognition of his outstanding support for the Medical Education and Community Orientation program. In 2006, he was honored by Lower Bucks Hospital for 40 years of service to humanity. He practiced medicine until February 2012.

Peter J. Gulden Jr., M.D. '65, Winter Park, Fla.; August 28, 2012. He served as a flight surgeon for the United States Air Force at Tan Son Nhut Air Force Base in the Republic of Vietnam from 1966 to 1967. After his service in Vietnam, he settled in Florida, where he practiced internal medicine.

Roger C. David, M.D. '69, Portland, Ore., an ophthalmologist; August 9, 2012. He was a founding member of Oregon Medical Eye Clinic and EyeHealth Northwest. During his medical training, he practiced general medicine on the Waggoner Indian Reservation in South Dakota. Later, he also volunteered in Guatemala.

'80s

Arthur V. Stein, M.D. '80, a plastic and reconstructive surgeon who had practiced in Allentown and Bethlehem, Pa.; July 16, 2012. He developed widely used techniques in hand reconstruction, and he created guidelines used nationally for office-based surgery certifications.

LEGACY GIVING

Alumna Rhoda Rosen Quietly Blazed a Trail for Women

When Rhoda Rosen, C.W. '54, M.D. '58, enrolled in medical school, it was a man's world – 99% of her classmates were men, with only six women in the entire class. This imbalance did not deter Dr. Rosen but spurred her on. After graduation, she became the first female resident in the Department of Obstetrics and Gynecology at Albert Einstein Medical Center and, later, the Center's first female surgeon.

One could easily describe her as a pioneer or a trailblazer, but she shrugs that off. "At the time I was just doing what I do," she says.

What she was doing was something rare, even in her own experience. Dr. Rosen did not meet a female physician until she went to medical school.

Throughout her 20-year career, she never forgot the place that gave her a stellar medical education or the fact that a mayoral scholarship allowed her to become a Penn undergraduate in the first place. Her gratitude inspired her to create a bequest that will ultimately benefit the Medical Class of 1958 Scholarship Fund.

"I feel that the medical school allowed me to flourish as a person and to achieve professional status," she says. "I thrived because of Penn."

Dr. Rosen notes that the bequest was a simple way for her to give, and she used a codicil to stipulate funds for the Perelman School of Medicine while still providing for her large family, which includes eleven grandchildren. She is passionate about telling other alumni that they should give back.

"Anyone who went to the School should realize that they would not be where they are today without the Penn education. I think that is a big motivation to pay it forward to today's students."

Philanthropy is certainly not the only bond Dr. Rosen has with her medical alma mater. She has served as class agent and chair of her class's Reunion Committee. Her participation was recognized in 2008 with the Alumni Service Award. Seymour, her husband of more than 50 years, attended the ceremony along with her four children.

Perhaps her greatest satisfaction comes from seeing the field formerly dominated by men has changed dramatically.

"I am thrilled to see that the gender gap is closing, and at least 50% of students at the School of Medicine are women," she says. "When I look back objectively, I guess I did help pave the way."

Dr. Rosen 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., senior director of Planned Giving, at 215-898-9486, or you can e-mail her at cewan@upenn.edu. For more information, please visit www.plannedgiving.med.upenn.edu.

A Different Kind of Personalized Medicine

Personalized medicine – using genomics to sort patients into smaller and more uniform groups and then treating them in a manner that will work best for each group – has been a goal for many years. Today, however, making such care available to a wider population is much more feasible.

In this issue, you can read about the new Center for Personalized Diagnostics, which provides a fuller – and more useful – genomic profile of patient's tumors (p. 2). And in "The First Word," Dean Jameson discusses some of the ways "big data" will continue to make personalized medicine more widely available and more precise.

Penn Medicine first covered the topic in the Spring 2008 issue, noting that as personalized medicine continued to develop rapidly, many of Penn's cancer specialists were taking the lead. As the authors put it, "To judge by the proliferation of reports in the media, including articles in both the professional and popular magazines, the Age of Personalized Medicine is already upon us."

But the *Penn Medicine* article also reported a certain amount of skepticism and public wariness, and the article cited a symposium held the previous year at Penn, organized by the Institute for Translational Medicine and Therapeutics. Its title: "Personalized Medicine: Boon or Pipe Dream?" Garret A. FitzGerald, M.D., director of the sponsoring institute and chair of the Department of Pharmacology, subsequently expressed some of the ambivalence about the "personalization" of medicine: "It is a seductive concept and easy to overhype. However, it is a highly complex task presenting medical, technical, social, and political hurdles. Its realization will occur in a stuttering fashion – rapid progress in some areas contrasting with frustrating delays in others."

In our Spring 2009 issue, we reported on another local symposium, hosted by the Penn Genome Frontiers Institute and the Franklin Institute. While advances were duly noted, the consensus of the speakers seemed to be that challenges still remained. Since then, the advances have continued, the technology has improved, and the costs have come down noticeably.

It was in this context that Ana E. Núñez, M.D., delivered last fall's Mossell Lecture, an annual event in honor of Nathan Francis Mossell, the first black student to graduate from Penn's School of Medicine. Núñez, a professor of medicine at Drexel University and associate dean for urban health equity, education, and research, spoke on the topic "Personal Enough? The Quest for Personalized Medicine and Health Equity."

In this time when personalized medicine has gained much support among health-care professionals and the general public, Núñez asked her audience to take a closer look at what it means – or *should* mean. She acknowledged the need for effective information systems and for getting "the right diagnosis and treatment of the right patient at the right time," but her focus was not on that kind of personalized care. Instead, she urged the students in the audience to pay very close – personal – attention to the patients they will be treating in a few years. It is the nature of medical education, Núñez argued, that it teaches stereotypes rather than individuals. "But then you get to patients," and the individuality becomes so important.

"Who Is This Person in Front of Me?"

Health disparities exist, Núñez asserted, but "we have an opportunity to make a difference." An important step is to understand that "one size fits all" does not work in the real world, where the socio-economic and cultural backgrounds of individual patients can vary tremendously. "We need systems where people can be human," said Núñez – in other words, systems in which the practitioner recognizes those differences among patients and tries to see "who is this person in front of me." That means taking into account sex, heritage, experience, and other important factors. During her medical training in Philadelphia, Núñez recalled, she knew to ask about a patient's home life, but she didn't ask, for example, whether anyone in the family was incarcerated. As she put it, research has shown that "trauma actually has an influence in changing genes." In the same way, she pointed out that the families of some patients may play a significant role in how patients are treated and how they fare.

"We have multiple subcultures," said Núñez, asserting that physicians must be aware of how these subcultures intersect with medicine. Physicians need to see both what is the same and what is different about their patients. "We are not experts in the lives of our patients," she said, which is why health-care professionals need "cultural humility."

Núñez also spoke briefly about what she called "personalized public health." One telling example she gave relates to the kind of food and the amount of food students in West Philadelphia's public schools eat. As she noted, there are no school lunches for such students during the summer. Their doctors should be aware of this important difference, which can have an impact of the students' health.

The "playing field" is not level for all players, said Núñez. The implication is that the presumed benefits of the high-technology personalized medicine may not be available to all patients, at least at first. But doctors and doctors-to-be can still provide personalized treatment. If they view their patients as complex individuals and "ask the right questions in the right way," Núñez concluded, they can make a significant difference collectively. ●

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Charles C. Branas, Ph.D., had been studying gun violence and its connection to geography and place since coming to Penn in 2000. "I really wanted to turn the corner and start doing something to *improve* health and safety." To do so, he's employed one of epidemiology's oldest tools – maps.