

Icing on the Cake: Kicking Off the Birthday Year

On September 8, under a large tent on College Green, the Perelman School of Medicine kicked off its 250th birthday year with a cake-cutting celebration. Leading the festivities were Amy Gutmann, Ph.D., president of the University of Pennsylvania President; 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; and Ralph W. Muller, CEO of Penn's Health System.

After their remarks, the cake-cutting began. For the hungry onlookers – faculty, students, staff, and alumni – there were three large cakes and 500 cupcakes, all decorated for the occasion with appropriate symbols and text.

A special guest for the celebration was the person Gutmann described as "the great benefactor," Ray Perelman. In 2011, with his late wife Ruth, Perelman pledged \$225 million to the medical school that now bears his name.

For his part, Jameson also saluted Rosemary Mazenet, M.D. '86, Ph.D. '81, who is serving as chair of the 250th anniversary committee. In his remarks, Jameson noted many advances in medicine over the years and predicted that the school would still be flourishing 250 years from now. He called it the first – "and still the best!"



President Gutmann is flanked by Ralph Muller (left) and J. Larry Jameson.



Left THE PREP

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- The Brain in Peril | By Marshall Ledger and Mark Wolverton Scientists and clinicians at Penn Medicine and elsewhere have been expanding our knowledge of the harm that sports and warfare can do to the brain and coming up with ways to detect and treat brain injuries sooner.
- 18 Symbols, Oaths, and Exhortations:
 The White Coat Ceremony | By John Shea
 At this year's White Coat Ceremony, incoming students heard about each other and an international project that keeps vaccines from spoiling in transit before they reach patient communities in rural areas.
- The Doctor Prescribes . . . Information | By Martha Ledger An alumna who blogs under the name Seattle Mama Doc believes that physicians today, especially those in primary care, must meet their patients where they are on social media.
- 2/ My Father's Three Birthdays | By Ronadip R. Banerjee Dr. Banerjee, M.D. '05, Ph.D. '03, an instructor at Stanford University, has written a personal essay about his father's illness as he navigates a vast and often impenetrable health system.
- A Man of Many (P)arts | By Karen Kreeger and John Shea A recent recipient of the John Scott Award for his scientific work on electron transfer, P. Leslie Dutton, Ph.D., professor of biochemistry and biophysics, is also an accomplished artist.
- The Role of Culture in Health | By Sally Sapega Each year, the University of Pennsylvania sponsors a series of events focused on a central theme. For the 2014-2015 academic year, the topic is Health, which also acknowledges the medical school's upcoming 250th anniversary.

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A Towering New Presence

Penn Medicine University City, the new outpatient facility on Market Street, was dedicated on September 12. Showcasing a new model for patient experience and engagement, the facility was developed with a \$38 million investment from Penn Medicine and in partnership with Good Shepherd Penn Partners, The University City Science Center, and Wexford Science & Technology. The 150,000 square-foot site is now home to more than a dozen clinical specialties whose staff work together in multi-disciplinary teams aided by state-of-the-art medical technology. Patients are provided a modern, "one-stop-shopping" clinic for outpatient services, an ambulatory surgical center, and a 29,800-square-foot therapy and rehabilitation facility.

With nearly 110 exam rooms, six outpatient operating rooms, and an outpatient medical imaging and diagnostic testing center, Penn Medicine University City serves as Penn Presbyterian Medical Center's most comprehensive ambulatory care site. Its location expands Penn's footprint within the West Philadelphia community, bringing more health-care services closer to where people work. The facility, located at 38th and Market streets, also serves as a new "front door" to Penn's campus from University City onto the growing Market Street medical and Science Center corridor, providing easier access for patients coming from West Philadelphia and the nearby suburbs.

According to Michele Volpe, executive director of Penn Presbyterian, "The lessons learned throughout the design and development process of this extraordinary facility will inform the work we do each day in our existing facilities, helping us to continue building upon our already rich culture of excellence and map new strategies to deliver the very best patient care."

A New Model in Patient Experience and Care Delivery

Penn Medicine University City's new patient engagement model is clearly demonstrated by the Penn Musculoskeletal



Center, the first enterprise of its kind in the region. The center offers a highly specialized approach to treating orthopaedic disorders, injuries and other conditions of the joints, bones, or muscles. Clinical specialties on site include orthopaedic surgery, rheumatology, physical medicine and rehabilitation, internal medicine, pain medicine, and therapy/rehabilitation services. The center will also be home to the new Penn Center for Human Performance, slated to open later this year.

"We're offering a whole new approach to integrated care," said L. Scott Levin, M.D., chair of the Department of Orthopaedic Surgery. "When patients are involved and knowledgeable about their condition and the management plan, both their experience and care are improved."

Developed using best practices from industry leaders in customer service, combined with feedback from Penn Medicine

A Rise in the Ranks

In the annual *U.S. News & World Report* survey of hospitals, a combination of Penn Medicine hospitals was named to the publication's 2014 Honor Roll. The Hospital of the University of Pennsylvania and Penn Presbyterian Medical Center were ranked the 7th best in the nation. Out of nearly 5,000 hospitals *U.S. News* analyzed, only 17 institutions were named to the Honor Roll, a distinction that signals "both rare breadth and rare depth of medical excellence," according to the magazine's editors.

In addition, *U.S. News* once again ranked Penn Medicine hospitals #1 in the Philadelphia area. Pennsylvania Hospital was ranked #6 and Chester County Hospital, the newest member hospital in Penn's Health System, was ranked #17 in the region.

Penn Medicine's rankings in 10 different specialties also rose, with eight areas named to the top 10 programs in the nation. These included Gastroenterology & GI Surgery; Ear,

Nose, and Throat; Geriatrics; Gynecology; Cardiology and Heart Surgery; Neurology and Neurosurgery; Pulmonology; and Urology.

In an e-mail to faculty and staff, Penn Medicine's leaders noted that *U.S. News* had made changes in the methodology used to rank hospitals' clinical specialties. This



year, for instance, the weight assigned to reputational score within each specialty area was reduced, while weight for each hospital's patient safety score was increased. Penn Medicine's improved ranking can be attributed in part to the perfect patient-safety scores (5 points out of a possible 5) it received. □

patients, the center offers a patient- and family-centered approach. For example, the Musculoskeletal Center provides each patient with a dedicated care coordinator, an innovative role that provides patients with a single point of contact for scheduling follow-up visits, additional tests, and referrals.

Upon arrival, patients visiting the center will be escorted by a concierge to small waiting rooms that group patients according to specific conditions. The center also offers added



services such as check-in kiosks, iPads loaded already with educational material specific to the patient's injuries, and large flat screens in exam rooms, to be used for clinicians to review and discuss imaging results with patients or offer patient education videos between visits with specialists.

Rehabilitation services are also a cornerstone of the facility, through Penn Therapy & Fitness University City. The facility contains Penn Medicine's first therapy pool, complete with an underwater treadmill and underwater cameras. The cameras allow therapists to give guidance and direction while watching the patient move. \Box

– Katie Delach

Blocking Autophagy Shows Promise Against Cancer

In the largest group of results to date, researchers from Penn Medicine's Abramson Cancer Center and other institutions have shown in clinical trials that the malaria drug hydroxychloroquine (HCQ) blocked autophagy in a host of aggressive cancers — glioblastoma, melanoma, lymphoma and myeloma, and renal and colon cancers — and in some cases helped stabilize disease. Autophagy, a process by which cancer cells degrade their own intracellular organelles, is required for cancer cells to fuel their growth. It is also a crucial troublemaker that spurs tumor growth. Block this pathway, many preclinical studies suggest, and anti-cancer agents such as chemotherapy and radiation therapy will be able to do their job better.

Results of six trials — five in humans (with more than 200 patients) and one in dogs — were reported in the May online issue of *Autophagy*. The author is Ravi

K. Amaravadi, M.D., assistant professor of medicine in the Division of Hematology/
Oncology and co-leader of the Cancer Therapeutics
Program at the Abramson
Cancer Center. He was the principal investigator on four of the six trials.

"These studies provide promising evidence that autophagy blockade can be achieved, and that combining autophagy inhibitors with other cancer therapies in very sick patients can

be accomplished safely in most cases," said Amaravadi.

The phase I and phase I/II trials aimed to measure the safety of adding HCQ to either chemotherapy, radiation therapy, or targeted therapies, HCQ's effectiveness in inhibiting autophagy, and the potential clinical benefit of HCQ combination therapies.

In melanoma, researchers observed prolonged stable disease in 20 percent of the patients on temozolomide. In another trial, researchers observed stable disease in 75 percent of patients with metastatic melanoma on temsirolimus. In the dog clinical trial, all 30 dogs with non-Hodgkin's lymphoma treated with HCQ and the standard chemotherapy doxorubicin had clinical benefit, and nine had complete remission.

Autophagy is a relatively new target in cancer, infectious disease, and neurodegenerative disorders. While advances in the fundamental understanding of autophagy are increasing at a breakneck speed, translation of these advances into clinical trials and clinical benefit has been lagging. More recently, HCQ has shown promise in treating pancreatic cancer patients in ongoing clinical trials; however, its tolerability and effectiveness to stop autophagy in humans with other cancers has not been shown before. \Box

- Steve Graff

OH

Hydroxychloroquine (HCQ

NIH Finds Significant Merit in Penn Studies

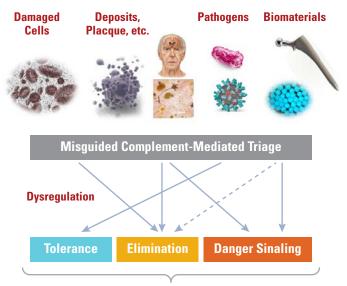
In an era when research funding is significantly harder to come by, four multiyear studies by Penn Medicine researchers, including two multi-university projects, will be supported by the National Institutes of Health.

One study, funded by the National Institute of Allergy and Infectious Disease, is a five-year, \$10 million renewal of a program project to study the oldest part of the human immune system, called the complement system or simply "complement." Complement, a network of more than 50 proteins in the blood and on cell surfaces, is part of the innate immune system. That is different from the adaptive system consisting of antibodies that can "learn" and adapt themselves on the fly to different antigens. The complement proteins quietly cruise the blood system, keeping a low profile until they are triggered into action.

John Lambris, Ph.D., the Ralph and Sallie Weaver Professor of Research Medicine in the Department of Pathology and Laboratory Medicine, is the lead investigator on the renewed program project. With his colleagues, he is developing novel therapeutics to tame inappropriate complement activation and to protect cell surfaces from an attack by this defense system.

Penn Medicine researchers are also part of a five-university collaboration seeking to identify rare genetic variants that may either protect against or contribute to the risk of Alzheimer's disease. The grant from the National Institute on Aging is \$12.6 million over four years. At Penn, the Consortium for Alzheimer's Sequence Analysis (CASA) is led by Gerard D. Schellenberg, Ph.D., professor of pathology and laboratory medicine. CASA investigators will analyze data from 6,000 volunteers with Alzheimer's and 5,000 older individuals who did not have the disease. In addition, they will study genomic data from 111 large families that have multiple Alzheimer's disease members to identify rare genetic variants.

"By identifying additional Alzheimer's-related genes, the CASA team aims to find new therapeutic targets that will reduce the economic and human burden caused by this disease,"



Inflammation, Autoimmunity & Infection

said Schellenberg. "This is an exciting opportunity to apply new technologies to improve our understanding of the biological pathways underlying this devastating disease."

The Scheie Eye Institute was awarded a five-year, \$11.2 million grant to study the genetic risk factors that make African Americans disproportionately more likely to develop primary open-angle glaucoma (POAG). POAG appears almost ten years earlier and progresses more rapidly in African Americans than among Caucasian individuals, making it the leading cause of irreversible blindness in this population. Approximately two million Americans suffer from this form of glaucoma. The primary investigator is Joan O'Brien, M.D., chair of the Department of Ophthalmology and director of the Scheie Eye Institute.

POAG is a group of diseases that cause progressive and irreversible retinal ganglion cell damage, optic nerve degeneration, and corresponding visual field loss. Once a sufficient number of nerve cells are damaged, blind spots begin to form in the patient's peripheral field of vision. Even when medical



Making Cancer Glow

Penn Medicine researchers are fighting cancer with color. Working with colleagues at the School of Veterinary Medicine, surgeons have developed a way to make lung cancer tumors flash neon green for better visibility during surgery. The procedure involves injecting patients with an FDA-approved dye, indocyanine green, 24 hours before surgery. The properties of the dye allow it to bind with receptors on cancerous tumors, causing them to fluoresce neon green under infrared light or near-infrared imaging.

Their glow allows surgeons to remove the tumors they can see with the naked eye and

feel with their hands, as well as those that may be too small or too far below the surface of the lung to view or feel. The team's latest study tested the procedure in 18 patients. "We were thrilled to find that the dye allowed us to identify and remove five additional tumors that we did not know were there," says Sunil Singhal, M.D. '98, G.M.E. '07, assistant professor of surgery and director of Penn Medicine's Thoracic Surgery Research Laboratory. "By removing these, we were able to prevent a local cancer recurrence and also reduced these patients' chances of developing metastatic disease." \Box

and surgical management are employed, retinal ganglion cell loss can be progressive and irreversible.

The risk of developing POAG increases tenfold when a parent or sibling has the disease, with even larger increases when an identical twin is affected. Said O'Brien, "By dissecting the disease into subtypes and understanding the different genetic underpinnings of the disease, we can begin to develop better, more targeted treatment options."

The goal is to conduct a comprehensive genetic analysis of POAG in African Americans. The genome-wide analysis will help identify the biological pathways and networks underlying the disease. "Our hypothesis is that genetic variants influence the risk of POAG and the traits related to that risk, such as intraocular pressure and corneal and retinal nerve fiber layer thickness. We believe that demographic and ocular risk factors and medical co-morbidities also contribute to the increased risk of POAG in African Americans."

Mesothelioma: Can Photodynamic Light Therapy Help?

Researchers at the Perelman School of Medicine are also collaborating with the Roswell Park Cancer Institute to study the effects of photodynamic light therapy (PDT) in patients with malignant pleural mesothelioma. This rare, aggressive, and deadly cancer most often manifests itself in the lining of the lungs and is caused almost exclusively by exposure to as-



bestos. The four-year grant of \$8 million from the National Cancer Institute will fund a clinical trial and additional studies looking at the effects of PDT on the patient's immune response, the tumor cell itself, and the blood vessels surrounding the tumor.

"Mesothelioma is a cancer for which there is currently little to no hope for a cure," said Eli Glatstein, M.D., the principal investigator of the program project grant and professor and vice chair in the Department of Radiation Oncology. "This trial represents a major step in understanding the combination of treatment modalities that will offer patients the best hope for survival and extended remission."

The study, which expects to enroll 102 patients over four years, will administer Photofrin – a photosensitizing agent that makes cancer cells more sensitive to dying from light therapy – to trial participants 24 hours prior to surgery. Patients will undergo a radical pleurectomy, which is the removal of the pleura or lining of the lung along with the tumor cells contained within. They will then be randomized to two groups: half will receive PDT intraoperatively via an intense laser inserted in the chest cavity during the surgery, along with post-operative standard chemotherapy; and half will receive only post-operative chemotherapy. Photofrin absorbs the light from the laser and produces an active form of oxygen that can destroy residual microscopic cancer cells left behind after surgery. Radical pleurectomy allows mesothelioma patients to keep their lung and is associated with better postoperative quality of life and improved survival compared with other common mesothelioma surgeries.

The second project will examine the process by which PDT works to destroy tumor cells and look at whether there is an agent – a drug or other therapy – that can boost its effects. The third project will look at whether certain pathways roused during surgery may play a key role in inflammation and cell growth and thus contribute to treatment failure in any way, and whether inhibiting these pathways will improve the efficacy of intraoperative PDT. Finally, the team will study the vasculature of the tumor in patients following PDT and evaluate any changes in the vascular environment as a result of intraoperative PDT and the potential for modulation to improve the efficacy of the treatment.

"This trial will help us understand how PDT works in the body and what we may be able to do in the future to improve the body's response to the therapy," said Glatstein. \Box

A Boom in Biomed Patents

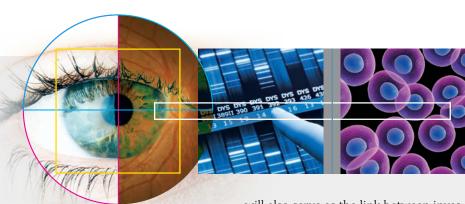
Over the past year, the Perelman School of Medicine has seen a tremendous increase in its innovation engine that drives patenting activity. In this period, the total number of new and follow-on patent applications filed increased 23 percent, from 351 to 456, and the number of patents issued to Penn and its faculty and staff inventors increased by 20 percent, from 58 to 70. It's all part of the Penn Center for Innovation's charge: to realize the potential of translating research into commercially viable products that save lives and generate economic benefits.

Case in point: James W. Wilson, M.D., Ph.D., professor of pathology and laboratory medicine and director of the Penn Gene Therapy Program, ranked number two among translational researchers in a recent survey by *Nature Biotechnology*, which tallied scientists' total patents at their current institution. Wilson's patents – according to the magazine, totaling 90 in the U.S. and Europe – include those for technology used in gene therapy based on different types of the adeno-associated virus (AAV). Gene therapy vectors relying on AAVs to carry corrective genes can be inserted into cells, and they persist in the human body without integrating into the host genome. AAVs produced in Wilson's lab have already been used by hundreds of institutions worldwide in preclinical and clinical trials for such disorders as hemophilia and lysosomal storage diseases. \Box

Penn Establishes an Ocular Therapy Center

Nearly seven years ago, Jean Bennett, M.D., Ph.D., Albert Maguire, M.D., and a team of investigators from Penn Medicine and The Children's Hospital of Philadelphia used gene therapy on 12 patients - including five children - who had Leber's Congenital Amaurosis, a disorder that causes blindness. The team was able to deliver a healthy version of the gene causing the disorder, RPE65, to the patients' retinas, ultimately leading to vision improvements in all 12 patients in the initial study. To help facilitate the development of such novel therapies for treating retinal and other ophthalmic disorders, Penn Medicine has created the Center for Advanced Retinal and Ocular Therapeutics (CAROT).

"A program like this unites all necessary approaches to researching and treating retinal and ocular disorders," says Bennett, the F. M. Kirby Professor of Ophthalmology at the Perelman School and director of the new center. (Maguire, professor of ophthalmology, is co-director.) "An important premise



of CAROT is to make the technologies that effectively advance research and therapies for the visually impaired and blind available to physicians, scientists, and patients."

Through its advanced research facilities and services, the center will extend these successful approaches developed for specific retinal or ocular disorders to support research on other disorders and advance therapies and cures for visual impairment and blindness through partnerships with others in ophthalmology, neuroscience, cell biology, and genetics. CAROT will function as a knowledge base to provide interested investigators with guidance on constructing vector gene therapy, designing clinical trials, and identifying and enrolling patients. It

will also serve as the link between investigators and existing core services at the University of Pennsylvania, the National Institutes of Health, Children's Hospital, and other institutions that provide genotyping and bioinformatics and other translational research services.

A recipient of the NIH Director's Pioneer Award in 2011, Bennett has been recognized for her innovative approach and potential to produce an unusually high impact on this broad area of biomedical research. As she puts it, "We believe the momentum we have established will allow us to develop an internationally recognized center and become the premier center in the U.S. for the personalized diagnosis and treatment of retinal and ocular conditions."

– Lee-Ann Donegan

Transitions

Kevin Mahoney has been promoted to executive vice president for the Health System and executive vice dean for the Perelman School of Medicine. He had been senior VP for the Health System and vice dean for the medical school. In the memo announcing his new appointment, Mahoney was praised for his management and leadership skills that have been visible in many critical projects that have supported the current success of Penn Medicine. He played an important role in developing the Center for Health Care Innovation and the Center for Personalized Diagnostics, as well as the move

toward developing a new bed tower on campus. He has also been a key partner with the University in developing the Penn Center for Innovation. Under Mahoney's leadership, UPHS has reached and exceeded many milestones, including federal designation for Meaningful Use in information technology. He also led



the complex negotiation leading to the Novartis Penn Alliance, the largest partnership ever between a university and a pharmaceutical company. Most recently, Mahoney is leading the construction of the Jordan Center for Medical Education and the significant expansion of the clinical facilities on the Penn Presbyterian campus.

Lauren Steinfeld, J.D., was named chief privacy officer for Penn Medicine and senior advisor on privacy. Serving in the Penn Medicine position on an interim basis since last September, Steinfeld led the overhaul of content in the training module on the Health Insurance Portability and Accountability Act (HIPAA). She also



provided orientation and guidance to several new privacy officers for the individual entities of the organization and handled several critical reviews of business associate agreements and coordinated investigations of alleged violations of HIPAA privacy.

Previously, Steinfeld was chief privacy officer for the University of Pennsylvania, working on privacy issues involving medical information, student records, electronic data, Social Security numbers, and other personal information. She was the first person to hold such a position in higher education. A Phi Beta Kappa alumna of the University of Pennsylvania, Steinfeld has also taught a course in Privacy Law at Penn's Law School.

Honors & Awards

Frederic D. Bushman, Ph.D., professor of microbiology, has been honored with a Pioneer Award from Human Gene Therapy for his early pioneering work. Bushman increased understanding of how HIV reproduces by inserting its genetic material into the DNA of a host cell, and that research led to crucial advances in the ability to move pieces of DNA and

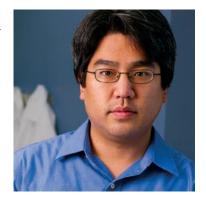


whole genes between cells. The journal is commemorating its 25th anniversary by honoring 12 leading pioneers in the field of cell and gene therapy, as selected by a blue ribbon panel. Each recipient has written a "Pioneer Perspective."

In "Engineering the Human Genome: Reflections on the Beginning," Bush-

man recalls his research as a graduate student and postdoctoral fellow studying the regulatory mechanisms that control gene expression and identifying DNA binding proteins that viruses such as the HIV retrovirus – use to integrate into a host genome at targeted sites. Bushman's research has contributed to the development of new gene-delivery vectors and to more effective and efficient methods of targeting them to integration sites.

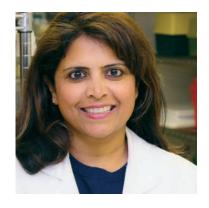
Edward B. Lee, M.D. '05, Ph.D., G.M.E. '04, assistant professor of pathology and laboratory medicine, has received a three-year Clinical Scientist Development Award for \$486,000 from the Doris Duke Foundation. The award will support his research in frontotemporal lobar degeneration and amyotrophic lateral sclerosis (ALS). Lee



heads the Translational Neuropathology Research Laboratory, which aims to understand the causes of neurodegenerative diseases in order to develop specific disease-modifying therapies. He will study a mutation in the C9orf72 gene, the most common genetic cause of frontotemporal degeneration and ALS. In 2012, Lee received an Excellence in Science Award from the American Society for Investigative Pathology.

Nishaminy Kasbekar,

Pharm.D., corporate director of Pharmacy Services at Penn Presbyterian Medical Center, was named Pharmacist of the Year by the Pennsylvania Society of Health System Pharmacists. The award acknowledges sustained contributions to all aspects of the profession. According to the Society,



Kasbekar "continuously shows her creativity and dedication toward the enhancement of clinical services within hospital pharmacy," as part of the administrative team at Penn Medicine. She has served as the organization's president.

Anna M. Moran, M.D., clinical assistant professor in the Department of Pathology and Laboratory Medicine, was named one of the American Society for Clinical Pathology's "40 Under 40" for her achievements in the medical laboratory field. She has served on several committees and councils for the Society.

Stefanie B. Porges, M.D., G.M.E. '92, clinical associate professor of emergency medicine, has been appointed to a threeyear term on the Disciplinary Board of the Supreme Court of Pennsylvania. She will fill one of the two non-lawyer positions on the board. The disciplinary board is an independent agency under the Supreme Court's jurisdiction, consisting of 13 members. It assists the Supreme Court in all matters involving attorney licensing and discipline in Pennsylvania. Porges currently serves as an attending physician in emergency medicine and as medical command physician for the PennSTAR Flight Program.

Marco Ruella, M.D., an associate in the Penn Institute for Immunology, received the SITC-EMD Serono Cancer Immunotherapy Clinical Fellowship Award. The one-year award, for \$100,000, is the first of its kind offered by the Society for Immunotherapy of Cancer. It is meant to support the development of the next generation of immunotherapy experts through dedicated funding of novel research. Ruella was selected as the winner for his project "Dual Chimeric Antigen Receptor T Cell Therapy for Human B-Cell Acute Lymphoblastic Leukemia." He was a postdoctoral fellow at Penn's Translational Research Program, led by Carl June, M.D. According to Ruella, the goal of his research is to treat patients who have relapsing or refractory B-cell leukemia with chimeric antigen receptor T cells that target multiple antigens, so that the tumors cannot escape. \Box



he Brain

Scientists and clinicians at Penn
Medicine and elsewhere have been
expanding our knowledge of the
harm that football and some other
sports can do to the brain – and
coming up with ways to detect and
treat brain injuries sooner. Although
concussions have drawn most of the
attention, a newer focus is chronic
traumatic encephalopathy, a
potential result of cumulative blows
to the head. In addition, Penn
researchers are working on ways to
detect and treat traumatic brain
injuries caused by battlefield blasts.

Photographs by Addison Geary except where noted

Peril

Football on Trial

Three physicians – all of whom once played the sport – consider the problems caused by a football-associated disease that is still largely a mystery.

By Marshall A. Ledger

ey, he's not wearing his Super Bowl rings." Like a lobbed forward pass, that whispered sentence floated over the audience gathered at the College of Physicians of Philadelphia earlier this year to hear a discussion of "Football: America's Pride or America's Shame?"

The panelists were just taking their seats, and the observation referred to the fingers of Douglas A. Swift, M.D. '80, G.M.E. '83, an anesthesiologist who had practiced at Pennsylvania Hospital. Swift played as a linebacker for the Miami Dolphins of the National Football League from 1970 to 1975; the team was the Super Bowl champion in '72 and '73.

Many in attendance might have gaped with awe and respect at seeing the rings (a goodly proportion had watched this year's Super Bowl), even though they had come to this event to learn about a grimmer side of the sport: the growing problem of concussions and their cumulative, disastrous effects on the brain in the form of chronic traumatic encephalopathy, or CTE – and on the slow uptake of professional football and of society in general to deal with the problem.

Swift was joined by H. Branch Coslett, M.D. '77, the William N. Kelley Professor of Neurology at Penn; and by Paul W. Butler, M.D., a retired general surgeon from Dover, N.H., whose proposal to end football at his local high school - because of the CTE risk - was almost universally condemned. Coslett and Butler had played football in high school and college, so they too had felt at first hand both the sport's demands and its joys. Now, like Swift, they are evaluating its costs.

Despite the current interest in CTE, it's far from new. It was first identified in boxers in 1928 and labeled dementia pugilistica or "punch-drunk syndrome." It was recognized as "progressive" in 1954, and its neuropathology was first described in 1973. The first positive diagnosis of CTE in a football player was published by Bennet Omalu, M.D., in 2005. Since then, CTE has also been found in those who play



Douglas Swift in the stands of Franklin Field.

hockey, baseball, rugby, and soccer, and in other athletes as well. A 2012 brain study at the Boston University School of Medicine found CTE in 33 of 34 pro football players tested post-mortem.

At stake for the National Football League, whose annual revenues are now about \$10 billion, is the nation's continued interest in the game. (The NFL is especially eager to retain the allegiance of the most valued TV viewers, those between 18 and 49 years old.) Also at stake: a constant and full pipeline of players starting before elementary school and extending through college, and the enthusiasm of parents for their children's participation.

Coslett opened the program by flat-out calling CTE an "epidemic" and a "plague." The brain, he noted, has a Jell-O-like consistency and resides in a hard shell with sharp edges. "Soft brain, hard skull - that's problematic if you get hit on the

head," he said. As it rocks back and forth inside the head, the brain "loses billions of the wires that connect nerve cells."

Coslett contrasted CTE to traumatic brain injury, which he defined as one or two very hard hits on the head. CTE, he pointed out, seems to emerge after countless smaller shocks in a process "that's not really known yet."

Continual impacts particularly affect the frontal lobes, which are associated with personality and behavior, among other functions. CTE seems to cause "a constellation of changes," said Coslett, including irritability, anger ("yet also apathy"), impulsive behavior, depression, and suicide – as well as memory loss, dementia, diminished executive functioning, Parkinsonism, and problems with speech and gait.

Yet CTE, so far, has defied scientific understanding. Boxing is full of "repeated smashes to the head in a sport where the aim is to smash someone in the head," said Coslett, but only 50 percent of boxers have CTE. "Why not the others? We don't know why," he observed, "and it makes it difficult to answer a [current] parent's question, 'Should my son play football?"

Nor can researchers explain CTE's gradual onset; or why some patients, and not others, recover from the blows; or



Douglas Swift's two Super Bowl rings.

which therapy is best, although, Coslett said, rest is currently the standard approach to reduce inflammation.

Some investigators are exploring potentially predisposing factors such as age, gender, "cognitive reserve," which plays a role in Alzheimer's disease as an ability to fend off brain damage, and (in the realm of molecular genetics) the apolipoprotein E (ApoE) gene, which in mutated form is a risk factor for Alzheimer's disease.

One promising research area, Coslett suggested, is the tau protein, which seems to be elevated in patients with CTE. Within the year, he said, new kinds of PET scans will examine the tau ligands, which will "light up tau in the brain. In principle, this should be good to identify tau deposits."

66According to H. Branch Coslett, the brain has a consistency like Jell-O and resides in a hard shell with sharp edges. "Soft brain, hard skull – that's problematic if you get hit on the head," he said. As it rocks back and forth inside the head, the brain "loses billions of the wires that connect nerve cells.

But he cautioned about false positives and false negatives. Some 30 percent of those who show Alzheimer's in autopsy showed no symptoms in life, he noted. "Now suppose you take the test and a little tau shows up" - what will such results mean?

"We really don't know how to interpret them," he pointed out. "This is going to create a firestorm" in the immediate future, he predicted. "This is going to be unbelievably controversial."

"The big question," said Doug Swift in his opening salvo, "is, 'Why, why would any sensible young man want to play football?"

In his own case, "it was fun," he said, "even, in some points, artistic." It gave him a community, with friends, coaches, and fans, along with his family, and it provided stature. He grew up in Syracuse, N.Y., and was nine when Syracuse University's team was voted the national football champion in 1959: "Therefore all the kids in town were national champs," he remarked.

He showed a photograph of himself back then in his Sherman Park Lions uniform ("it gave instant credibility," he said): a kid's physique with exaggerated facial fierceness. He was trying to emulate the photos of the pros, even to the point, he noted, of scrunching his neck down to make it look thicker.

Swift also enjoyed the athleticism that football demanded, and he wasn't shy about the need to be rough. He quoted approvingly an observation by George Stade, Ph.D., a polymath English professor, now retired, at Columbia University: "The mode [of football] is violence, and violence is its special glory." (Stade has also referred to a perfectly executed football play as an "aesthetic experience.")

In the locker room, Swift said, the preferred word was hitting, adding, "This was the part of the game that I really loved." He was taught how to hit, to be aggressive, "to deliver a message" to opposing players, and to ignore the bruises. He pointed out that Malcolm Gladwell, writing in The New Yorker in 2009, called this aspect of participation "gameness," where you go all-out for those in charge — coaches or mentors or trainers. Swift likened it to boot camp in the Marine Corps and, perhaps more surprisingly, to "the exhausting rigors of residency" in medicine.

Gameness could come near to being a "spiritual quality," Swift acknowledged. He cited a football player who crushed an opposing ball carrier in a tackle and, when asked how it



felt, said, "It felt warm all over." Swift said he himself liked to "channel the sentiment" expressed by Low Dog, an Oglala Lakota chief on the day of Little Big Horn: "This is a good day to die: follow me."

At the same time, Swift indicated, he did not always glory in the results. What he called the "worst play" he was ever involved in was a tackle of a Baltimore Colts pass receiver, Ray Perkins, who was knocked out on a play and went into seizures. (Perkins did recover and went on to a 40-year coaching career).

Swift also gave a brief history of football from its origin in rugby to a more precise and defined style of play - for instance, in the line of scrimmage, where offense and defensive teams directly confront each other. (That formation invites repeated subconcussions - linemen reportedly get knocked on the head more than 1,000 times each season, no matter what level of play.) The new rules were in keeping with American culture and science, he said, leading to the "strategic complexity" and specialization of today's game, which ramps up the need for coaching, preparation, and equipment.

Swift said that he recognized the real risks – for instance, children of quite different sizes competing in the same football league - yet he looked back on his own experience with fondness. The sport had been especially good to him in supporting his education, he said, even after his professional

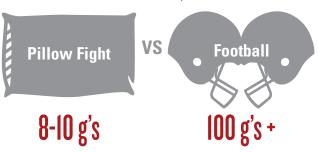
career. "I'm certain that my role as a football player played a good part in getting me accepted into medical school."

The third speaker was retired surgeon Paul Butler. As the moderator, George M. Wohlreich, M.D. '79, the director and CEO of the College of Physicians, put it in introducing him, he "attained unwanted fame." In 2012, Butler became aware of recent research on CTE, including the article by Omalu, whose autopsy findings of the pro player Mike Webster drew widespread attention. Among the interested groups was the

66 Defenders of football argue that helmets are harder and thus safer. In response, Paul Butler pointed out that harder helmets may prevent skull fractures but do not reduce the kinetic energy transmitted to the brain, which continues to move until it strikes the inside of the skull.

WHEN KIDS PLAY

Accelerometers measure the G Forces from a hard hit on 7- to 9-year-olds



National Football League, which tried to get Omalu to withdraw his study before it had been published.

Butler concluded that children should not be playing football, that other activities could instill values such as self-confidence, hard work, and the sacrifice of self for the team, values often associated with the sport. Even more, he came to believe that it was "morally unacceptable" to offer it in the public schools.

At the time, Butler, who had practiced surgery for more than 30 years, was a member of the Dover, N.H., school board. He sent his accumulation of studies and articles to the board's six other members, requesting any writings that might refute their conclusions. He received no response, and when he brought the issue to a vote in 2012, he lost, 6 to 1. Still, his proposal reportedly "upset the community."

(A comparable face-off occurred at the University of Pennsylvania in February 2013 when Malcolm Gladwell, delivering a speech at the invitation of the Benjamin Franklin Scholars, addressed the CTE issue and called for high schools and colleges to shut down their football teams. Referring specifically to the post-mortem diagnosis of early-stage CTE in the Penn football captain who committed suicide in 2010, Gladwell urged students to "boycott football games at Penn." The proposal stirred controversy on the campus for days afterward.)

To the College of Physicians audience, Butler pointed out that football, unlike other sports, uses the head "as a weapon, both as a battering ram and as a spear." Children are especially vulnerable because most between 6 and 13 years of age "have relatively big heads and weak necks, like bobble-headed dolls." He cited research that showed that accelerometers in the helmets of 7- to 9-year-olds have registered 100 g's and more. In comparison, a vigorous pillow fight can product 8 to 10 g's; heading the ball in soccer, 25 g's; opposing football linemen typically hit each other with a force of 30-35 g's.

Defenders of football argue that helmets are harder and thus safer. In response, Butler said that harder helmets may prevent skull fractures but do not reduce the kinetic energy transmitted to the brain, which continues to move until it strikes the inside of the skull. By contrast, he noted, automobiles are safer with softer front ends, which crumple and absorb energy in a crash.

Yet Butler recognized what he called the spectator's "essential conundrum": "Most of us fans like to see the big hits. But most of us hate to think that someone will get hurt."

CTE is not football's first survival crisis, Butler noted. In 1905, when 19 football players died of their injuries, the sport was nearly abolished by "top-down" actions of some university presidents and the reproach of President Theodore Roosevelt.

At present, the impulse for change may be "bottom-up": from the parents of today's schoolchildren who are part of the "risk-averse" Generation X. Many of them favor amber-alert protocols, "baby on board" signs, and five-point restraint systems for children's car seats. As they gain a wider understanding of CTE, "the pipeline for football players will dry up," Butler predicted, because "their children will have other things to do than to crack their heads together on the football field."

In the question-and-answer session, the panelists agreed that changes in rules could reduce the potential for "calamitous" injuries but that hitting would still be its central feature – or the game would be so tamed that no one would want to watch it.

Asked whether they would encourage relatives to play football, the panelists were unanimously negative. Football nowadays

Another Voice

Gary W. Dorshimer, M.D. '81, was not a speaker at the College of Physicians of Philadelphia event but he is an expert in sports medicine who has treated many patients with concussions. In addition to his regular duties as chief of general internal medicine at Pennsylvania Hospital, Dorshimer is head team physician for the Philadelphia Flyers of the National Hockey League and team internist for the NFL's Philadelphia Eagles. Dorshimer is encouraged by the recent international standardization of guidelines for dealing with concussions as well as the growing public awareness that athletes should be removed from play promptly when concussion is suspected. On the other hand, he asserts that the cause-and-effect relationship for chronic traumatic encephalopathy has not been "well worked out" yet. "I take care of a lot of ex-athletes that don't have any higher incidence of neuro problems than the general population." At this year's Winter Olympics in Sochi, Dorshimer was an internal medicine consultant for the NHL. Many of the European physicians he met there, he says, "are skeptical of the help from neurocognitive tests in diagnosis and treatment, and I think they are waiting for more solid info

At this point, Dorshimer has a more positive view of sports and its attendant risks than the speakers at the discussion. "I think we can't keep putting fear into their lives without also showing the value of sports, mentally and physically, at all ages. Because for the majority of people, concussion is not a long-term doom-and-gloom scenario, and the values of exercise, teamwork, etc., can have short- and long-term value to many more people than those that will be hurt." The ratio of risk to benefit, he believes, must be weighed. — Editor

is "way over-intensive," said Swift. Referring to his grandchildren, he added, "Certainly I would discourage football," but hoped they would find other "sport-like endeavors."

Butler, in turn, was vehement: "I would do whatever I could to keep my grandchildren from playing, short of . . . you know . . . getting myself kicked out of town."

Noticing the Elephant: Penn and Traumatic Brain Injury

By Mark Wolverton

It's not just in football and other professional sports culture that the pernicious effects of traumatic brain injury (TBI) are finally being acknowledged. Doctors are realizing that even a single mild concussion can have lasting effects on a person who's never set foot on a gridiron.

"It's been this elephant in the room that's finally been discovered," notes Douglas Smith, M.D., director of Penn's Center for Brain Injury and Repair and the Robert A. Groff Professor and vice chairman of research and education in the Department of Neurosurgery. "People now recognize that a concussion is more than just mild traumatic brain injury. There's nothing mild about it, since we have shown that about 20 percent of the cases have persisting cognitive function impairment – they don't go back to school or work."

Under Smith and his colleagues, Penn's Center for Brain Injury and Repair has become one of the world's leading facilities for research into TBI. According to D. Kacy Cullen, Ph.D., research assistant professor of neurosurgery, "Penn is one of

the few locations that really has attained the crucial critical mass to be able to investigate these issues all the way from the most basic level to the patient level. It's just a very comprehensive, integrated approach that is using some established models but also some very new technology and new techniques."

The increasing awareness of TBI is helping to drive new research initiatives. "The incidence of concussion seems to be

going up tremendously, but that's really just about reporting," says Smith. "Previous clinical studies in TBI have all been mostly severe cases and a little bit of moderate injury, and what's wrong with those is that those patients have what we call very heterogeneous injury." Because some severe TBI patients might manifest brain swelling, others massive bleeding, still others large contusions, statistical comparisons are difficult. But it's now known that such severe cases make up only about 10 percent of all TBI patients, Smith notes, "and that number is going to be shrinking because concussion is becoming reported more and more."

That sharply increased level of reported mild cases is important, because it allows closer study of the 20 percent who suffer lasting effects from TBI. According to Smith, "If we can

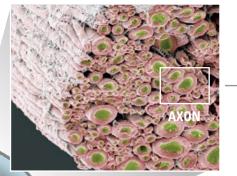


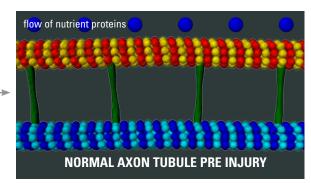
Douglas Smith, shown here with research specialist Andrew Jaye, investigates telltale changes of axonal injury in patients with mild concussion.

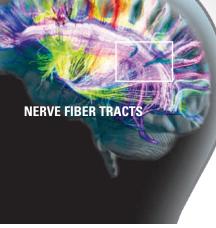
identify who they are, then we don't have to worry about using a particular treatment or looking at a rehab paradigm on everybody — and then have it be just meaningless because 80 percent were going to get better anyway. This way we can identify that 20 percent who are likely to have persisting symptoms and split them into groups to test approaches and therapies."

TRAUMATIC BRAIN INJURY

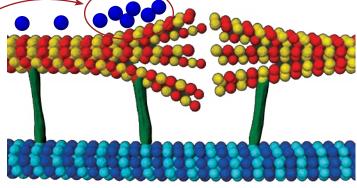
Below illustrates the effects of axonal injury following a traumatic brain injury.







After traumatic brain injury, microtubules inside the axon that carry vital proteins are broken. Those proteins spill out, causing swelling that can then disconnect the axon, which can lead to neuronal death.



AXON TUBULE POST-TRAUMATIC BRAIN INJURY

Those patients in the 20 percent are being scrutinized through several complementary approaches at Penn. Based on the predominant pathological model of concussion that is centered on damage to the axonal cells of the brain (the precise mechanisms of which were discovered and defined by Penn researchers back in the 1980s), Smith and his collaborators are using advanced neuroimaging such as functional MRI to

Douglas Smith and his collaborators are using advanced neuroimaging such as functional MRI to look for telltale changes of axonal injury in the white matter of mild concussion patients. The idea is to develop sensitive tools that will help scientists try to correlate the injury with the patient's neurocognitive status.

look for telltale changes of axonal injury in the white matter of mild concussion patients. Researchers have used MRI to look at changes, "not just in the white matter but in the brain function," says Smith. The idea, he explains, is to develop sensitive tools that will identify the extent and distribution of the axonal pathology so that scientists might be able to try to correlate with the patient's neurocognitive status.

But mild axonal injury sometimes escapes even advanced MRI and CT examination. "I call it stealth pathology," Smith says. To get around that problem, Penn scientists are developing another promising diagnostic tool, a blood biomarker that can reveal axonal pathology with a simple blood sample. "The damaged axons will actually start to degenerate and release a fragment of a specific protein that's really only found in axons, created by a pathological process that we previously characterized," explains Smith. "It's still early, but thus far we had almost 100% identification of patients in the acute setting. The ones where we saw this peptide were also the same ones that had persisting symptoms."

A third approach examines patients not for physical damage but for functional impairment, using sophisticated neurocognitive assessments that can pin down specific behavioral problems caused by brain injury. As Smith puts it, "They really fit the overall picture that there might be more obvious neuroimaging changes, neuropsychological tests that we can give these patients acutely, and a blood biomarker. The triad of studies with these patients can help identify those who are going to have long-term problems."

An intriguing possibility being suggested by the increased number of reported cases is that some people may have a genetic predisposition that increases their vulnerability to TBI and/or their chance of suffering lasting effects after an injury. "I joke that the number one genetic risk factor for getting a concussion is the Y chromosome – reckless behavior," Smith says. "However, the interesting fact is that while boys or even men might have more exposure, it turns out that girls have a higher rate given the same sport." Thus, another area that re-

searchers area interested in investigating is why girls have a higher rate of concussions as well as what appears to be a worse outcome in the long run. In addition, girls take longer to recover than boys. "If there's that kind of a difference," says Smith, "there really may be a true genetic component to this – meaning that certain individuals may be predisposed to that outcome.

Those findings also raise the prospect of identifying especially vulnerable individuals before they're exposed situations that would put them at risk. "Maybe before you get to sign up for football, you have to have a clean bill of health showing that you don't have genetic markers that might predispose you to a bad outcome if you had a concussion."

By studying what happens on the cellular level during TBI, Penn researchers are also investigating how even a single concussion can lower a person's damage threshold for future injury. When axons are severely damaged internally, it's not only the transmission of nerve signals that's affected. If the microtubules inside the axon that carry vital proteins are broken, those proteins can spill out, causing other problems. "Everything keeps piling up and the axon swells out to the point

66 Maybe before you get to sign up for football, you have to have a clean bill of health showing that you don't have genetic markers that might predispose you to a bad outcome if you had a concussion. 99

where it will actually disconnect," Smith says. He points out that it is not the axons that break apart at the time of injury but the microtubules that can break. In turn, that break causes swelling that can then disconnect the axon. "And once disconnected, that connection is gone forever."

Even worse, however, is that such damage to the axons can also increase the long-term chances that the individual will develop neurodegenerative diseases such as Alzheimer's disease. When axonal proteins accumulate in the wrong places, they can eventually lead to amyloid beta plaques and tau tangles, hallmark signs of Alzheimer's. "When we looked at brains of people who had a severe brain injury and died within hours of injury, we see about a third of those individuals have diffuse amyloid beta plaques," Smith notes. "They could be a teenager and they would have plaques that you would find typically in an older individual."

Tau tangles, on the other hand, take longer to appear. "That's also been looked at with boxers and obviously now with football and rugby players and almost any kind of sport players who've had repeated exposure. Because of the way their exposures are, we don't exactly know the time course for that." But with a single severe injury, Smith explains, the tau tangles take about a year to appear. Smith's laboratory is currently working on a Defense Department grant to look at the evolution of tau pathology.

Smith emphasizes that in the case of a concussion, the vast majority of people get better. But the heightened risk, especially for football players and others exposed to repeated mild TBI, is not to be discounted. "So many people want their kids to be a football hero, but how much are you willing to put on the line for a game?" he asks. "People ask me, why is it getting so bad? It's not getting bad, it's always been bad. We've known since 1928 that boxers have early dementia. And soon afterwards they found all these brain pathologies. It seems like there shouldn't be any mystery that in any sport where you hit your head over and over, you're going to have a similar type of problem."

After years of neglect, the problem is finally getting the attention it deserves. Sometimes, however, that attention comes in the form of legal initiatives. In August, parents of soccer players in the United States filed a class-action lawsuit against FIFA, the international governing body of soccer, in an attempt to force changes in the protocols for dealing with concussion. In July, the NFL agreed to remove a \$675 million cap in the settlement for compensating former players for concussion-related claims. The original settlement specifically set aside \$75 million for baseline testing and \$10 million for medical research and education. Earlier in the year, the National Collegiate Athletic Association and the U.S. Department of Defense announced a \$30 million initiative to enhance the safety of student athletes and members of the military services. According to the sponsors, it will include the most comprehensive study of concussion and exposure to head impact ever conducted. In the meantime, researchers like Douglas Smith are encouraged. The good news in the field, he says, "is that with this new strategy that we've developed to look at clinical trials, I have crazy high expectations that we're going to have success really early. This new awareness about concussion gives us a study group to make it better."

Kacy Cullen shares Smith's optimism. "There's been a sea change in public consciousness about TBI." Moreover, he notes that, for decades, Penn has been on the leading edge of research efforts and patient care in TBI. "We're well positioned to stay on the leading edge for the foreseeable future."

The Wounds That Don't **Show: Traumatic Brain** Injury and the Military

By Mark Wolverton

In the past, American soldiers did not have to worry much about traumatic brain injury, specifically concussions from blast effects. "Historically, if you were exposed to blast, it would be pulmonary injury that would be fatal," explains D. Kacy Cullen, Ph.D., research assistant professor of neurosurgery. "In fact, all of the [Department of Defense] lethality



Kacy Cullen and other Penn researchers are investigating exactly what happens to the brain when it's exposed to an explosive shock.

curves for blast that were generated in the '60s were based on thresholds for lung injury." To put it in starkly morbid terms, most soldiers who were subjected to blasts strong enough to cause TBI were already killed by other injuries. Little attention was given to TBI.

"There's a famous saying in warfare that generals are always fighting the last war," says Cullen. He believes the same thing can be said for the medical management. "Clinical treatments and soldier protection are based on the last war, so you're inevitably unprepared for anything new because it's impossible to anticipate everything."

The recent Iraq and Afghanistan conflicts have indeed brought something new and unanticipated. Ironically, while the widespread use of high-tech body armor to protect soldiers in battle has saved countless lives, it's also made warfighters more vulnerable to other dangers – specifically, TBI.

"Although the body armor improvements were designed to mitigate ballistic projectiles, they have conferred some degree of protection for lung injury," says Cullen. "The body armor has allowed soldiers to survive and has shifted that mortality threshold to a point where the brain is vulnerable but the blast itself is not lethal."

PERCENTAGE OF ALL INJURIES CAUSED BY BLAST WWI + WW2 + Korea + Vietnam = 3%

The New Lethality

In all 20th-century wars, blast caused less than 5 percent of injuries. (Some estimates are as low as 2-3 percent). But in Iraq and Afghanistan, Cullen says, it has been responsible for two-thirds of the injuries. "The blast exposure itself is much more common, and the soldiers are surviving more powerful blasts due to shifts in the lethality curve." In addition, be-

cause of better medical management, more soldiers are surviving in general.

Douglas H. Smith, M.D., director of Penn's Center for Brain Injury and Repair, elaborates: "The signature injury of the recent conflicts has been mild TBI or concussion." It follows that the DOD and the Department of Veterans Affairs are very interested in these topics. "The VA is going be responsible for taking care of these service people for years to come. It's going to make Agent Orange look like nothing, just by the numbers."

Complicating the situation is that mild TBI or concussion resulting from a blast from an improvised explosive device (IED) or similar weapon can be devilishly difficult to diagnose, especially in the presence of other more obvious injuries. While most concussions among civilians are the result of something hitting the head or vice versa, blast-induced TBI may involve no such mechanism, which masks its signs and symptoms.

As Cullen explains, very often the subject does not look physically harmed. "There could be shrapnel, there could be some type of superficial injury, but by and large these are just concussive blasts that the soldiers seemingly recover from, at least from a gross physical standpoint." In such cases, soldiers may be returned to duty as soon as they have regained their wits - certainly within a few days. But, notes Cullen, they may have persistent cognitive symptoms.

How to Detect the Impact of Blast

To address this problem, Cullen collaborated with Smith and Shu Yang, Ph.D., professor of materials science and engineering in Penn's School of Engineering and Applied Science, to develop a "blast badge." A patch that can be worn anywhere on a soldier's uniform, the blast badge changes color in response to explosive shock waves. Inspired by the iridescent sheen observed in nature in butterfly wings and bird feathers, the blast badge is composed of photonic nanocrystals sculpted by laser to form an intricate molecular structure. If struck by a blast shock wave, the structure is damaged, changing the wavelengths of light it reflects and thus its visible color. But the badge resists any other kind of physical impact or stress, responding only to explosive shock.

"We're able to tune it to change color within a shock-wave range that is consistent with survivable blast exposure," Cullen explains. The change of color occurs specifically because of shock-wave propagation, which allows an observer to immediately assess a soldier's specific exposure to blast and possible injury. "This technology can be tuned to those blast levels that may cause very subtle neurodegeneration that can't be appreciated by any biomarkers or imaging right now." Furthermore, the blast badge may make it possible to screen soldiers and move them out of harm's way. It could also give solders time to heal or allow physicians to provide any early intervention therapeutics "that would have a better chance of taking hold before you have fully blossomed neurodegeneration."

In addition to the blast badge, Cullen and other Penn researchers are investigating exactly what happens to the brain



when it's exposed to an explosive shock. "My lab is focused on looking at the inceptive events – what happens at that moment of blast exposure, whether it's just a shock wave or a more severe blast where the subject could be thrown and could have head rotational injury or impact injury as well. Blast injuries can be very complicated as you move from the mild-moderate to severe. But we're studying specifically what happens at the cellular level at the moment of blast exposure which is inducing a complex neural trauma."

Cullen and his lab are also working closely with the Philadelphia VA. He reports that he has a lab at the nearby VA as well as one at Penn. Injuries from blast, he emphasizes, "might be the biggest issue facing the VA over the next 50 years."

As in the civilian realm, the new awareness of blast-related brain injuries in military personnel is changing research and treatment paradigms. "There's been a tremendous amount of resources put into getting ahead of this," Cullen says. "I think we're on a good trajectory." □

Symbols, Oaths, and Exhortations: The White Coat Ceremony



n mid-August, medical students in the Class of 2018 were officially initiated into the Perelman School of Medicine and began "an exhilarating, memorable, and very challenging journey." Those were the words of Gail Morrison, M.D., G.M.E. '76, senior vice dean for education, who presided at the annual White Coat Ceremony.

Penn's first such Ceremony was in 1996, only a few years after it was introduced elsewhere. As described by Morrison, "The ceremony is meant to be a time to reflect on what it truly means to be a skilled physician – one who is not only knowledgeable and skilled in procedures, but also one who recognizes the importance and necessity of building a caring, trusting, and collaborative relationship with patients." The short white coats that each entering medical student receives show them to be physicians-in-training. But, Morrison continued, entering the Perelman School of Medicine also means joining a program that emphasizes humanism.

Humanism, she said, "is not only a fundamental value of our profession, but may be the most important or fundamental value in becoming a doctor. . . . Though making students knowledgeable and skillful is something we do really well, we, their teachers and mentors, must also assure that they will not, during their education, disregard the primacy of the doctor-patient relationship and the importance of being, at all times, compassionate, empathetic, and caring."

Donning the white coat was not the only symbolic event at the ceremony. As each student was coated by Morrison and Stanley Goldfarb, M.D., G.M.E. '75, associate dean for curriculum, they also received one of the most well-known instruments of medicine, the stethoscope. These were funded and presented by Louis A. Matis, M.D. '75, a member of the Medical Alumni Advisory Council. Then, after the coating, Jon Morris, M.D., associate dean for student affairs, led the students in another universal recognized ritual – taking the Hippocratic Oath.

The incoming class of 165 students (55 percent male) is drawn from 60 different undergraduate colleges and universities across 33 states. About 60 percent declared science as their college majors. Almost two-thirds of the students took

one or more years after college to engage in a variety of experiences before coming to medical school. Many of them pursued other interests in that time, working at the National Institutes of Health; doing research at top academic health centers; volunteering abroad in health clinics for the underserved; working in the pharmaceutical and biotech industries; or serving with Teach for America. Several of the incoming students have already published and presented articles in journals and at national conferences.

Humanism in Action

Each year, as Morrison put it, "we select a faculty speaker who we believe exemplifies the humanistic physician." This year's speaker was Harvey Rubin, M.D., Ph.D. '74, professor of medicine in the Division of Infectious Diseases and director of the Institute for Strategic Threat Analysis and Response. ISTAR



Louis Matis, M.D. '75, presents Ezinnem Ugoji with a stethoscope.

is a non-profit organization affiliated with Penn that is dedicated to educating the public, elected officials, and leaders from around the world on emerging threats to national and international security, with an emphasis on global public health.

In his talk, Rubin encouraged the students to choose action, to choose engagement with the world and its people. By doing so, he said, "you are choosing to engage, you are choosing a path that rejects indifference." He quoted Elie Wiesel, the survivor of the Nazi death camps and winner of the Nobel Peace Prize: "to be indifferent to suffering is what makes the human being . . . inhuman."

Part of Rubin's talk focused on a life-giving project that began in a small way. A few years ago, he received an e-mail from a friend, David Morse, the actor, who had just seen on TV a child in Haiti who was dying of diphtheria. "David asked me why, in this day and age, should any child die of diphtheria, especially since we have good vaccines against this gram-positive scourge. We talked about the loss of infrastructure in the earthquake-devastated island and how vaccines must be kept between 2 and 8 degrees Celsius - no lower and no higher - to remain effective." But, he continued, "the ability to keep vaccines

DEMOGRAPHICS OF THE INCOMING STUDENTS















at the proper temperature – from the manufacturer all the way to the last mile to the infant – was broken, not only in Haiti but all over the developing world." According to the World Health Organization, an estimated 3 million children under the age of 5 die of vaccine preventable deaths every year. That's when Morse challenged Rubin to "solve the cold chain problem."

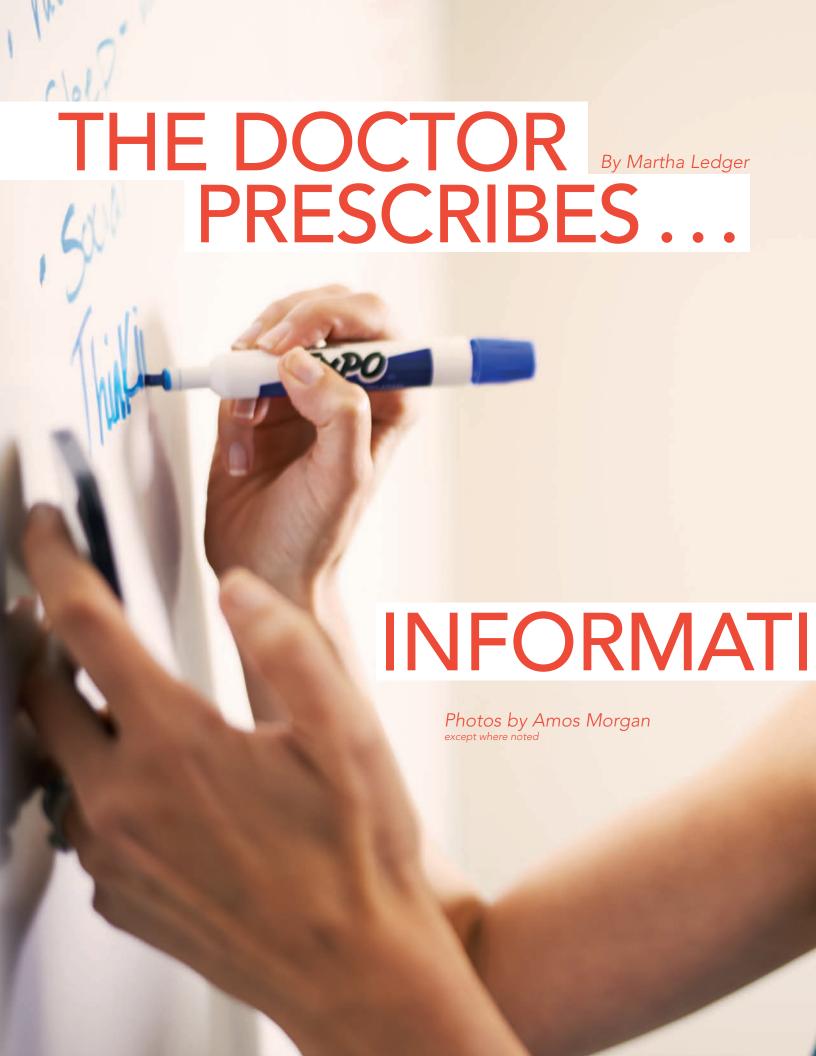
And Rubin – with many others – has started to do just that. The solution hinges on the fact that, even in remote parts of the world, many people have cell phones. "The private mobile phone industry is one of the most rapidly growing industries in the world, with complete global coverage expected within a decade if not sooner." To have a working cell phone, Rubin pointed out, you must also have a cell tower not too far away. "And that cell tower has a constant energy supply. If the private sector allows power to go out at the tower site, their business falls apart, so they have every incentive in the world to keep the energy flowing." With one of his students, Alice Conant, Rubin published a short paper in 2010 in New Scientist in which they suggested that vaccine refrigeration systems could be plugged into the energy supply of the cell tower cheaply and readily. "The solution is sustainable, scalable, and locally managed. And guess what – it works." Thus, Energize the Chain, a not-for-profit technology service company, was created.

With funding from Econet, a large mobile phone operator in Africa, Energize the Chain is functioning in 110 sites in Zimbabwe, where they were able to vaccinate more than a quarter of a million children. They expect to expand to another 100 sites in the coming year and another 100 in the following year in other African nations.

Despite this inspiring success, Rubin said, "We have a long way to go to create an even more robust vaccination program." He is now on the board of directors of Energize the Chain (http://www.energizethechain.org/), which works with both mobile network operators and several philanthropic organizations.

In concluding his remarks, Rubin said, "You are now on the Penn team, but remember who you play for – you play for *humanity*. Go and learn and make your mark." □

- John Shea





According to this Penn Med alum, physicians, especially those in primary care, need to meet their patients where they are – on social media.

Vendy Sue Swanson, M.D. '03, M.B.E. '03, has always had a lot to say. The Seattle-based pediatrician tells this anecdote about a vacation trip her childhood family and some friends took to northern Minnesota when she was still a pre-schooler. She would talk in succession and energetically to her mother, father, siblings, and the family's friends until each was thoroughly worn out and had had enough of her. After one such verbal marathon, her mother found her squatting over the ground, still blabbing away. "Whatever are you doing?" she asked. "Talking to the ants," Wendy answered.

Putting an idea or feeling into words is something Swanson does well. Over the last five years, she has poured out her medical knowledge and parenting concerns as Seattle Mama Doc, a blogging pediatrician who is also the mother of two young boys. (Her husband is Jonathan O. Swanson, M.D. '03, a radiologist at Seattle Children's Hospital and an assistant professor of pediatric radiology at the University of Washington.) You may come to hear a lot more about her, probably not as an advisor on teething or thumb-sucking (though her advice on these and other subjects is available online at seattlemamadoc.com), but as someone suggesting how doctors might use social media to better serve their patients.

At a very basic level, Swanson has upped the flow of information between herself and the public (both her patients and non-patients). In blog format, for example, she talks about such topics as vaccines, sunscreens, car seats, and tantrums, nimbly sliding from personal experience to practical information supported by well-done studies. She's engaging as a writer and frank as a medical expert, confident in what she knows and honest about what she didn't know. She believes that easy access to high-quality information can improve the delivery of medical care and promote healthy living. Her work may signal something more — an early wave of what some predict will be a patient revolution and a new model for doctor-patient relationships.

In addition to her blog, whose entries number more than 520 (as of September 2014), Swanson is a weekly medical contributor to KING 5 News in Seattle, an NBC affiliate; a frequent

speaker at conferences; and an active presence on both Twitter (she was named to *Time* magazine's Best Twitter Feeds of 2013) and Facebook. She has made around 75 short informational videos that are available on her site under the heading Seattle Mama Doc 101. In March, the American Academy of Pediatrics published *Mama Doc Medicine*, a compilation of her blogs. *Publisher's Weekly* called the book "practical as well as personal." In a blurb, Richard Besser, M.D. '86, chief medical editor for ABC News, describes it as "evidence-based advice on so many of the questions parents raise. It is packed with practical information; loaded with facts and tips to let you make informed decisions about your child's life."

Swanson is a Fellow of the American Academy of Pediatrics. In addition, she is on the board of advisors of the Mayo Clinic Center for Social Media, which, in 2010, became this country's first social media center focused on health care. In 2013, she was made executive director of digital health at Seattle Children's Hospital, where her charge is to provide electronic tools and communications know-how to other doctors.

Swanson didn't make a beeline to medical school, and her eventual hybrid career is not all that surprising. After graduating from Kenyon College in Ohio, she taught middle school for two years as part of the Teach America program, and she experienced the challenge of getting information across. When she eventually did arrive at Penn to study medicine, she was simultaneously drawn to bioethics and completed a master's degree in it along with her medical degree. She did her

Swanson spoke at the Paragon Health conference in 2013.

residency at the University of Washington/Seattle Children's Hospital in pediatrics because it seemed to her the right specialty for someone who wanted to help people and who had strong people skills.

While Swanson's current, multi-faceted communications career wasn't pre-planned, the delivery of health information

If It Were My Child: No Football for Now : APRIL 9, 2012



This is a position post where I take a stand that represents no one other than myself as a mom and a pediatrician. The reason I clarify this is that my position is a strong one. No one wants to go up against someone like the NFL, it seems. But let me say this very clearly: It if it were my child, I'd never let them play football. No way. For my boys, the risks are too large, the sentiments too cruel, and the gains simply not worth it. . . . This isn't just about the risk of concussion.

has long been on her radar. There was always something about the performance aspect of on-air reporting that fascinated her, she says. (It's not irrelevant to note here that Swanson, herself, has star quality: telegenic looks, intensity, poise, and verbal agility.)

At First, a Wariness of Media

As she recalls, however, there was a real wariness of media both in medical school and in her bioethics program. "We were kind of reared to distrust pharma, payors, and the media. There was a sense that those inside of medicine, who were saturated with health and medical knowledge, were very different from the people talking to the public about medicine."

During residency at the University of Washington, Swanson focused a now-critical eye on health reporting. She sometimes went with physician experts to the local TV station and sat in on their interviews and then felt frustrated when their informed responses were whittled down to sound bites.

Toward the end of her residency, Swanson gave a presentation on how media is not helping to change children's health. It was her first serious foray into the weeds of coverage, and she discovered additional culprits. A 2002 study published in JAMA showed that when medical journals issued press releases, they didn't routinely highlight the limitations of a study or the role of industry funding. These non-nuanced documents were then turned into potentially misleading news stories. Coverage of medical meetings was similarly problematic: Researchers would give preliminary data that – despite (or lacking) caveats – were reported as something close to a cure. In the end, the public didn't get the full story or get the story right. Health and medical reporting, she notes, only worsened during the latest recession, when experienced writers were replaced by less expensive reporters who often didn't even have undergraduate degrees in science. She recognized the enor-



One way Swanson gets her message out is through videos. Here she is with Evan Briggs, a videographer for Seattle Children's Hospital.

mous need for reliable health information, and she wondered if there could be better handholding between those in charge of media and those practicing medicine.

Swanson considered a public role for herself, but definitely not one outside her area of expertise. "I didn't want to be a pediatrician on the news talking about heart surgery," she says. She began seeing patients at the Everett Clinic, a forprofit, physician-owned, multi-specialty practice in suburban Seattle. In the process, she learned what it is like to be a primary-care doctor in the kind of health setting found all over the United States.

Vaccines: Telling the Real Story

She was a full-time pediatrician there in 2007 when Jenny McCarthy, a former model, actress, anti-vaccine activist, and former co-host of the daytime ABC TV show *The View*, appeared on *Oprah* and said she believed that the measlesmumps-rubella vaccine had caused her son's autism.

In clinic the next day, Swanson saw a mother and her 12-month-old. "I was going to give her daughter that vaccine plus the varicella-co-administered-with-hepatitis-A vaccine," she says. "I kind of rattled them off. The mom bit her lip and looked right at me and shook her head. And I said, 'Did you see Oprah yesterday?' And she said, 'Yeah."

In 2008, Swanson proposed to the marketing department of Seattle Children's Hospital that she write a blog under its sponsorship. She maintained that the community needed somewhere to go where they know there's a doctor talking, someone who can present the best available evidence on critical subjects, such as vaccines – someone, that is, "who can tell the real story." The hospital agreed to pay Swanson for her writing time, and she cut back on clinical practice to two days a week. The blog came online on November 11, 2009. "May we make change. Help others find their way to do what is right for their kids," she wrote, adding what set the tone for her subsequent entries, "Just like we're trying to do every day in my house."

In her first full year of blogging, Swanson wrote 134 essays on such subjects as her son's learning how numbers work; the frustration of swim club wait-lists, which concluded with a heads-up about chlorinated pools and infant bronchiolitis; the need to restructure snacking; the anterior fontanelle on a baby's skull as a focal point for parental anxiety; "chivalry" versus real career opportunities for women (she highlights Elizabeth Blackwell, the first woman to receive an M.D. degree in the United States [1849], who was not allowed to practice in this country); and the need for rear-facing car seats until a child reaches two.

When Swanson took up blogging, lots of people were already telling their own medical tales online. Facebook, patients' sites, and the mommyblogosphere provided forums for non-medical people to tell about their medical experiences.

This Will Not Change Pediatrician Resolve: JULY 28, 2014



I live as far away from Florida as any continental American (you do the math) yet Florida politics this past week affect pediatricians and families everywhere. In my opinion, every parent should tune in and follow this case. Florida just restricted physician free speech and hindered a physician's ability to help your neighbors, your relatives, and your family create a safe environment for children. . . . Florida may have gotten this wrong thinking that restricting a pediatrician's words and inquiry about safely storing firearms meant that pediatricians were trying to take away guns. Not so fast. . . . In 2011 I explained the gag-order for pediatricians — basically it's this: Florida says it's illegal for pediatricians to ask about how families and guardians store firearms in their home even though we know about 4,000 American children die every year from firearm injuries.

"Individuals' stories of illnesses and treatments were bubbling up in a powerful and provocative way," Swanson recalls, and she acknowledges that the stories were often compelling.

The Changing Role of Primary Care Doctors

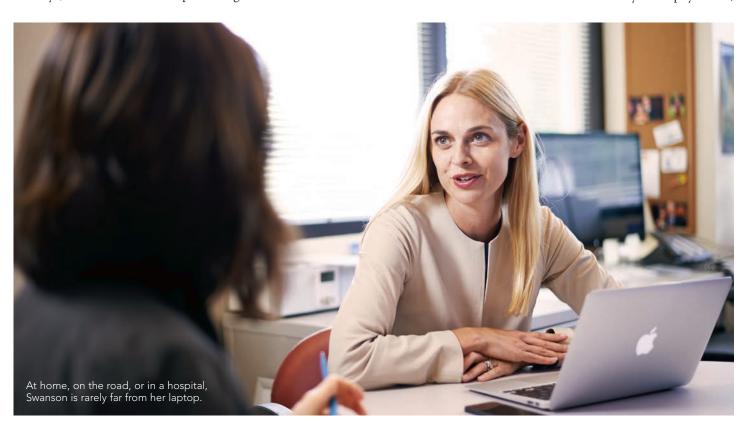
Despite their poignancy and power, however, such stories have a potentially serious downside. "What happens," Swanson says, "is that the teller's experience gets confused with

expertise." McCarthy's story of her son, for example, went against all scientific evidence. Nevertheless, it had the power to change a family's understanding of vaccine safety and maybe change the trust that family had in what its pediatrician was advising.

The rise of the Internet as a source of health information roughly paralleled the acknowledged national crisis in primary care. As medical journalist Shannon Brownlee details in her 2007 book *Overtreated* (the chapter titled "The Doctor Isn't In"), reduced reimbursements, burdensome paperwork, and utilization reviews – all fruits of managed care – thinned and hobbled the ranks of first-line caregivers. Many of these physicians had left or were leaving practice. Others retrained for more lucrative specialties or, dissatisfied with what the career had become, combined practice with other work. (That is what Swanson did. She is now practicing only one day a week, though her job shift is intended to improve primary care rather than escape it). All trends reduced the amount of time the remaining caregivers could spend with patients.

Swanson believes that some of the current ills of primary care (for both the beleaguered doctor and the short-changed patient) can be alleviated through an intelligent use of new communications technology.

It's known that patients are already online for health information (1 in 3 U.S. adults and nearly half of all college-educated adults, according to the Pew Internet & American Life Project). The Pew report also noted that 75 percent of people used a search engine first rather than a specific health site. At a minimum, Swanson wants physicians to direct patients to web sites that have been written or vetted by other physicians,



like MayoClinic.com or WebMD.com, or, for parenting information, her own, seattlemamadoc.seattlechildrens.org.

Swanson believes that physicians can also educate patients, listen and respond to them, or reduce some layers of off-putting bureaucracy — respectively and just for examples — by making short informational videos, adding a Q & A to their web pages, or by joining Facebook, so their practice managers can announce when flu shots have arrived.

But, in a more central adjustment, she wants to free of-fice-visit time by letting electronic technology handle the redundancy in primary-care practice – the non-personalized health and prevention information that the practitioner repeats many times a day. For example, the reminder about rear-facing car seats until the age of two. Swanson would like physicians to deliver this kind of information in a video – ideally one that physicians themselves make – that can be e-mailed home, accessed on the web, or even viewed on a tablet in the waiting room. It would be short – a minute in length – and unscripted. Doctors would simply recite "the schpiel" they routinely deliver in office visits for children younger than two. Having this important information delivered electronically would allow more time for conversation specific to the particular child.

A small collection of such videos could totally change the nature of, say, a routine six-month-old check-up, Swanson points out. It would contain an explanation of the growth chart, advice on introducing solid food, information about changes in sleep habits between then and the next visit at 9 months, and recommendations for vaccines. "What if I sent all that home a week before the appointment?" she asks. "Imagine how different the visit could be and the kinds of questions parents might have if they were more informed coming in to an appointment." She believes it would make the visit much more enjoyable for the physician as well.

Information transmitted by video actually has a better chance of making an impression than a verbal exchange in the office. Studies have shown that only 15 to 20 percent of what's said in the doctor's office is actually retained anyway. On the other hand, videos can be re-viewed, if necessary.

Patients Want Expertise

In primary care especially, Swanson says, "we will all have to function in some ways in a one-to-many format. We just can't afford to provide care the way we do now. We don't have the time we used to have."

But simply conveying information isn't enough. Swanson wants the physician to be the disseminator. "Patients don't want data," Swanson says. "They want *expertise*. They want access to what their chosen doctor knows and believes. They want that doctor to assimilate and humanize the data to help them make good decisions." Swanson's blogs often draw comments from those she is trying to inform. For example, "Something in the Air: It's Measles" (April 1, 2014) had 18 comments – as well as 8 responses from Swanson. Although not all the comments are positive, this one is fairly typical: "I simply love your blog, especially your frank yet kind-hearted

and compassionate advice on immunization. The measles outbreaks are so scary AND preventable. Thank you for taking the time to inform people like me."

"I gave a talk when I was a resident," says Swanson, "arguing from a bioethics point of view that you shouldn't answer the question that families always ask — 'If this were your child, what would you do?" She worried then that answers might prove too coercive or, made on the spot, not reflect the data.

But she has done an about-face on this issue. If someone in clinic asks what she would do about vaccines if it were her own son, she answers, "That's easy. My son did get his MMR shot on time." Online, she has a whole series of posts headed "If This Were My Child."

She would also like to see a continuing flow of information from specialists about specific disorders. A pediatric gastroenterologist, for example, could post whatever new findings there were – about, say, celiac disease – in just a few lines or through a link to the published study. "The patient can check in once or over a lifetime," Swanson says. She cites the Vaccine Education Center (www.chop.edu/service/vaccine-education-center/) created by Penn pediatrician and vaccinologist Paul A. Offit, M.D., of The Children's Hospital of Philadelphia, as a great example of doctor-supervised electronic information. "It is [primarily] parent-focused, presents his understanding of vaccine science, and is constantly being updated."

Simplifying Health Care: DECEMBER 3, 2013



It feels like I was born at just the right time for my work in health care. I completed my medical training just as social tools were percolating out to the masses. Motherhood and my practice of pediatrics auspiciously coincided with the bounty of information that technology has distributed, offered up, and shared unlike ever before.

I can search and learn about health wherever I am — at the park or in the walls of my own clinic or home. For me, using my phone, Twitter, my blog, apps, Facebook, activity tracker, and patient online communities to provide health care, consume it, and engage in it is my new reality. It turns out, amidst all the clutter and stress of health care reform and our reduced time with our own doctors, I can see clearly that intuitive ways of learning about science wed with thoughtful technology will let us care, cure, and prevent illness and injury like never before.

Swanson is looking for system-wide change. In our interview and also in a blog entry called "Dr. Google: Tips for patients who diagnose online," she notes that fee-for-service, fee-for-quality, or productivity-based delivery models are extremely wary about doctors and patients communicating anywhere other than in the exam room. In most such practices, e-mail is prohibited and doctors are forced to bring patients



Swanson signed copies of *Mama Doc Medicine* at an American Academy of Pediatrics event.

into the office when, she implies, it's not always necessary. Insurers reinforce this "sclera-to-sclera" mode of practice by not reimbursing for electronic communication. In many practices, the Internet – which Swanson uses for illustrations and to understand where a patient has gotten information – is, on purpose, unavailable.

This is not the case everywhere. She notes that at Kaiser Permanente (a pre-paid system), doctors and patients routinely e-mail one another, and physicians can even make telehealth visits.

Interestingly, at Kaiser, where the use of e-mail was mandated from the top down, doctors initially pushed back, expecting they would be inundated with trivial and bothersome questions. That didn't happen. Instead of increasing workload, e-mail actually reduced office-visit volume. The icing on the cake was a 2010 in-house study showing that electronic messaging between patients and physicians was associated with statistically significant improvements in patients' glycemic, cholesterol, and blood-pressure levels.

Not Laughing Anymore

In terms of practitioners, Swanson has sensed a shift in tone among her colleagues: "In the beginning," she recalls, "they laughed at what I was doing – 'You were going to be an academic doctor and now you're writing a blog!' But then they stopped laughing. Next, there were excuses – mainly, 'I don't have the time that you have." But now, Swanson says, some physicians are starting to say, "How can I do more?"

The task at hand, Swanson believes, is for primary-care givers, specialists, and even clinical researchers to become more public about what they know and more active in sending information out to patients through social media. "People al-

ready do their own Internet research before going to the doctor," Swanson says. "And the reality is that sometimes we [doctors] don't know more [about some specific thing]. Plenty of times families have brought in concerns about a vaccine issue that I didn't know anything about until I heard it from them and went and looked it up."

The goal for Swanson is to create partnerships with patients and enable what is termed "shared decision-making." Herein lies the revolution!

Physicians are already committed to social media – the technology that is driving the revolution. According to a 2011 survey by QuantiaMD that was summarized in the AMA's newspaper *American Medical News* in September 2011, physicians are well ahead of the general adult population (90 to 65 percent) in their use of it. Their use, however, is almost entirely personal or professional (contact with colleagues, medical organizations, etc.). What they don't yet do is use social media to communicate with patients.

To become public and transparent is a new role for physicians. Bryan S. Vartabedian, M.D., a popular blogger and pediatric gastroenterologist at Texas Children's Hospital who has taught classes with Swanson on the online identity of physicians, has written about it in a somewhat challenging tone. In a blog entry titled "Intimacy, Mission, and a Physician's Public Role" (September 27, 2013), Vartabedian writes that participating in an interconnected world will demand much from

Something in the Air: It's Measles: APRIL 1, 2014



We get confused with all the attention paid to these outliers [celebrities opposed to vaccination]. We forget that about 9 out of 10 parents in the United States DO immunize following their doctor's recommended schedule. We forget not a single study finds an alternative schedule is any safer. We forget that unvaccinated and under-vaccinated kids are at risk for preventable disease. We get confused how stories like this make us feel and we ditch what the science tells us. We forget that when we immunize ourselves we protect our body, the children too small to be immunized, and those at high risk for severe infection.

physicians and that most are now ill-prepared to deliver. Social media, he argues, calls for a public presence, one created around something that drives or inspires an individual. Physicians will need to stand for something and "declare themselves in a meaningful way."

That is what Swanson does through all her channels of communication, and she is ready for "peer-to-peer" health care. In her words, "It's rich, and real, and extremely valuable." □

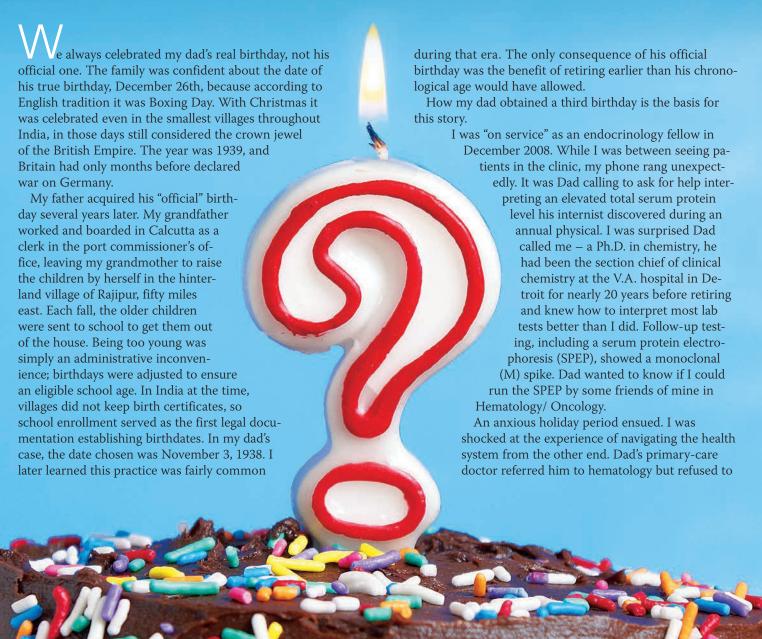
For more on the blog visit seattlemamadoc.com



My Father's Three Birthdays

When his father, section chief of clinical chemistry at a VA hospital, is diagnosed with multiple myeloma, an endocrinologist must make use of his medical expertise as they confront the vast health-care system.

By Ronadip R. Banerjee







Surath and the author, then one year old.

Surath Banerjee on a Galapagos cruise (2008).

order any testing or imaging in advance. The earliest appointment we could obtain was several months later! I ended up throwing my weight around as a physician and made phone calls to expedite things, but felt guilty because I knew most patients did not have that ability.

Then, on New Year's Eve, we sat in the local oncologist's office in Tucson and heard the unequivocal diagnosis: multiple myeloma.

That year turned all of our lives upside down. Our phone conversations became filled with details of chemo cycles and cataloging the side effects that were often worse than the disease at the time. The M-spike came down rapidly, but at the price of painful neuropathy. I

pored over every lab and data point, determined that the man who had financially and emotionally supported me through so many years of medical training would benefit from it all. I came to resent complaints from patients I saw in clinic who had minor medical issues. While my being a physician often helped Dad get better attention and care, it also complicated it, exemplified by an overly tentative bone-marrow biopsy

performed by colleagues that took more than an hour instead of minutes.

My dad's diagnosis of incurable cancer instilled in all who loved him an oppressive sense of helplessness and frustration. He remained determined to fight but accepted his fate, consistent with his philosophical upbringing as a Hindu. But the scientist in him was never satisfied by the lack of an explana-

tion for what caused him to have such a rare illness.

It was frustrating that, despite my scientific and medical training and his own scientific knowledge, I could not articulate the arbitrary nature of certain things we "know" in medicine in contrast to the way scientific knowledge is accrued. No amount of

discussion seemed to satisfy. He wanted to know why and what to do. Physicians presented us probabilities and piled stressful treatment decisions on him and my mom in the name of patient autonomy. Myeloma provided no satisfying specific reason or cause that he could rationally grasp – he had had no environmental exposure, and he had paid careful attention to diet and exercise his whole life. Before the diag-

66The bad news came like a hammer to the chest. I stared in disbelief at the survival curves that dove down an exponential cliff – median survival for those relapsing within a year after autologous BMT was less than a year.

nosis, he had never even been on daily prescription medications. It seemed tremendously unfair and made my mom and me very angry.

I convinced Dad to come to my own institution, Stanford University, for a second opinion. To our surprise, although he was 70 years old, he was offered an autologous bone marrow transplant (BMT). Dad decided to proceed mostly because of the possibility of several years free from continuous

chemotherapy before the inevitable relapse. At the time he was among the oldest patients to undergo BMT at Stanford. He was determined to continue his active retirement of golfing and international travel and chafed under the restrictions chemo cycles imposed.

On the morning Dad received the reinfusion of stem cells, the nursing team brought out a large colorful poster board calendar of the month, which they then taped to the wall. The date was highlighted: October 19, 2009. "You get a new birthday with your transfusion!" said the nurse. My dad smiled. "You can never have too many birthdays," he said. Now he had three.

Six months later we received the good news — blood work and bone-marrow biopsy confirmed he was in complete remission! He felt stronger each month, and I knew he was feeling better when he started to plan his next international trips. I moved forward at work euphoric. I met my future wife,

Ron and Surath in Ecuador (2008)

66 It was frustrating that, despite my scientific and medical training and my father's own scientific knowledge, I could not articulate the arbitrary nature of certain things we "know" in medicine in contrast to the way scientific knowledge is accrued. He wanted to know why and what to do.

wrote a grant, and made progress on my research projects. By that summer, Dad and I played a round of golf together. He had regained almost all of the pre-transplant weight, and although he drove the power cart instead of walking, he looked as he had before the myeloma diagnosis.

The bad news came like a hammer to the chest. At the annual post-transplant evaluation, a small but detectable M-spike appeared. He had re-

lapsed. In a frantic late-night literature search on PubMed, I found a review by a clinical research group at the Mayo Clinic on survival after relapse in myeloma patients following BMT. I stared in disbelief at the survival curves that dove down an exponential cliff – median survival for those relapsing within a year after autologous BMT was less than a year. I despaired over the facts of my dad's prognosis but decided to keep them to myself.

By the following spring, I was visiting Tucson every month. Chemo held the M-spike level stable but it did not decrease. A horrible case of shingles left Dad in unremitting pain, reminding me of the dictum that the efficacy of medicines is inversely proportional to the number of agents for any given symptom - and there are many painkillers. It was torture



Surath in the early 1970s

to watch the slow decline of a patient with terminal cancer. I had seen it as a medicine resident, and here cancer was gnawing away at the vibrant man who had been a pillar of strength for his family. But throughout he never wavered in his calm demeanor, and even at his worst physically he maintained an aura of inner grace that was so characteristic. Always the scientist and man of action, he plowed forward in planning an itinerary for a final trip to India in the fall.

My fiancée and I started arranging a wedding for the late summer. But the myeloma became resistant to the chemo. The M-spike doubled every few weeks, and Dad was "transfusion dependent." And then, almost miraculously, the addition of thalidomide seemed to melt the tumor away. It was ironic that a drug I had learned about in high school as the cause of horrific birth defects was responsible for extending my father's

life. After a brief hospitalization, Dad was no longer transfusion dependent. But even so, over the months he appeared to have aged decades. Dad vowed never to be hospitalized again.

My wife and I were married on Labor Day, September 5, 2011. It was a magical day and night – for 24 hours the weight lifted and Dad ap-

peared better than in more than a year, energetic, as usual the center of the discussion at the family table.

In early October, just weeks after returning from our honeymoon, my wife and I made our first visit to my parents' home as husband and wife. My dad insisted that I bring an old poster from a high-school genealogy project out of the closet and watched as I added my wife's name to the family tree tracing back over seven generations to Rajiv, our ancestor who had founded my dad's ancestral village. "We had a saying in the village," Dad said, "that the old leaves must fall to make room for the new ones." He looked tired but agreed to continue receiving the blood transfusions that kept him alive — until the end of the calendar year.

Less than a week later I was home again. I saw his face, the subtle changes in wrinkles on his face, the slight drooping of one eyelid, and heard the change in the timbre of his voice. He had lost one of his greatest traits – his articulate, precise speech.

Crying softly, I said, "Dad, you've had a stroke. I think it's time to stop." He closed his eyes for a moment, then opened

As soon as he could, Surath returned to the golf course (2010)

com, I passed the nights in a strange twilight sleep. We settled into attending to the grim practical business of the end of life; I finally understood the meaning of "attending physician.

them with a look of relief. Slowly with his left hand he traced the lifeline on his left palm, stopping where the crease ended between thumb and forefinger. For the first time in over a year he slept peacefully for twelve straight hours through the night.

We called hospice the next morning. I was amazed and grateful that within a few short

hours the hospital bed and supplies arrived. It was one of the few times the medical system had exceeded our expectations.

Day and night blurred together. On the hide-a-bed in the living room, I passed the nights in a strange twilight sleep. We settled into attending to the grim practical business of the end of life; I finally understood the meaning of "attending physician." Soon, Dad became bedbound. He seemed stoic and determined but weary.

After years of hoping and struggling to find any possibility of treatment and cure, I understood death as a release from the prison of a body irreversibly damaged by disease. Each night, as I stared up at the slowly spinning ceiling fan and listened to its dull humming, I was horrified to find myself praying that Dad would pass peacefully in the night.

Late the next afternoon, the hospice nurse arrived for her daily visit. "It won't be long now," she gently assured my mom and me in whispers outside my parents' bedroom. That afternoon, for the first time in several days Dad was quite alert and laughed joyfully during a sponge bath. In my youth, Dad had told me stories from old Hindu texts describing "wish-death," when noble and deserving sages are granted the boon of dying peacefully simply by wishing it. I was always rather dubious about its value. But as he looked at me wearily that evening, I implored him, "Dad, if you believe in wish-death, now is the time. I love you."

Some time that night he slipped into a coma. The following day, he died.

My father is the only person I have known that had three birthdays. The day he died, a few days short of his "official" 73rd birthday, he had just passed his second post-transplant birthday. He was not yet 72. Not a young man, but it seemed an untimely death, nevertheless.

I remember how I sneered at papers we read in internal medicine residency that trumpeted new treatments, especially in oncology, that extended life several months. My friends and I would roll our eyes, perhaps with good reason, based on our experience of some horrific deaths on the inpatient oncology wards. But I can say from personal experience that a couple of months in a person's life can make a tremendous difference, not just to the patient but especially to their loved ones who must learn to live without them eventually.

Many people have written about the problems facing the health-care system. I myself complained about a lot of them during training, especially the practical ones – scheduling,



judgment of what to do.

Son and father after Surath's blood marrow transplant (2009)

administrative duties, an overburdened system. But we have yet to address the root cause, the failure to articulate to patients what we are trying to achieve and what is the best way to get there. If a scientifically educated man with a physician son cannot easily navigate the decision process of modern medicine, how can the typical patient? We have presented patients with many "treatment options" and we try to assess

patient "satisfaction," but patients and families are not satisfied when we present probabilities rather than our best judgment of what to do.

Looking back, I think Dad struggled to balance his strong beliefs in fate and the philosophical traditions of Hinduism with his personal striving for knowledge, liberal thinking, and modern scientific training. It once seemed contradictory to me that such a rational thinker

would utter "Durga Durga," invoking the goddess favored by Bengalis when leaving the house for trips, yet criticize the "village mentality" that traps people in old ways for the sake of tradition. But although there always seems to be an eternal conflict between science and religion, fact and faith, for my dad these things never seemed to be in conflict.

"We are born alone and we die alone," Dad would often say to me, whenever we discussed loneliness or frustration within the limitations of human relationships. I never had a good response to that. It always seemed disrespectful to argue with someone who had accomplished a great deal from such a disadvantaged background with very little help, but it seemed too pessimistic from someone who was so serene.

This past year, I spent my first Father's Day as a dad myself. I never imagined that I would not be able to share that experience with my own dad. But that was not our fate. I have

last few months already **66**We have presented patients with displaying fierce looks of determination and flashes many "treatment options" and we try to of a knowing grin that I recall only too well. assess patient "satisfaction," but patients and families are not satisfied when we present probabilities rather than our best

Finally, I have an answer to his statement about the loneliness of human existence. Yes, Dad, we are born alone and we die alone. But we don't have to live alone. And though none of us escapes the real-

watched my child over the

ity of death at the end of our journey, all of us have the choice of how to live. Through all that you taught me and all that you shared with me, I have a father, friend, teacher, and mentor who remains with me as long as I live. \Box

Ronadip R. Banerjee received his M.D. and Ph.D. degrees from the University of Pennsylvania School of Medicine. He is currently an endocrinologist at Stanford University School of Medicine, with a research interest in diabetes.

A Man of Many (P)arts

By Karen Kreeger and John Shea

ART Illustration by NCS Studios Les Dutton, former chairman of the Department of Biochemistry and Biophysics, has been honored for his work as a scientist. He is equally comfortable in an artist's studio.

t the awards ceremony for the 2013 John Scott Award, held at Philadelphia's historic American Philosophical Society, Les Dutton made some rather grand claims in accepting the award. "We are now at the proof-of-principle stage of constructing our own man-made proteins that promote or retard electron transfer as needed for a variety of applications." Manmade proteins? Is this a visionary speaking? True, the award has been presented to such luminaries as Mme. Curie, Thomas Edison, and Jonas Salk, and Dutton is well known as an expert on electron transfer who has studied how electrons are organized in cells and how they convert light or oxygen into energy for the cell. He continued, citing two examples: "Man-made proteins with the properties for oxygen transport and the promise of stable inexpensive blood substitutes are in hand." Why stop there? He then suggested that advances in this kind of technology may one day be able to correct genetically inherited diseases in children.

"These are ideas still in the realm of fantasy," Dutton went on to say. It was a concession, but a somewhat grudging one. He reminded listeners that only 15 years ago, "the very thought of an iPhone would've been considered fantasy." It seems we are standing at the edge of another fantastic journey, another giant step for science. But, as Dutton reminds us, those steps can only be taken when much of the basic work in the field has been accomplished.

Les Dutton, Ph.D., formally known as P. Leslie Dutton, is the Eldridge Reeves Johnson Professor of Biochemistry and Biophysics, the director of the Johnson Foundation for Molecular Biophysics, and former chair of the Department of Biochemistry and Biophysics in the Perelman School of Medicine. After earning his doctorate in biochemistry at the University of Wales in 1967, he came to Penn the following year – and has been here ever since. The John Scott Award is by no means the only honor he has accrued in his career. Named a Fellow of the Royal Society in 1990, he is also a Fellow of the University College, Wales. Germany's Max Planck Institute presented him with the Frontiers in Biological Chemistry Award, and he has received the IBM Partnership Award. From Oxford University: the Senior Visiting Fellowship. From Cambridge University: The First Sir William Dunn Scholar.

He is also an accomplished artist, but more on that later.

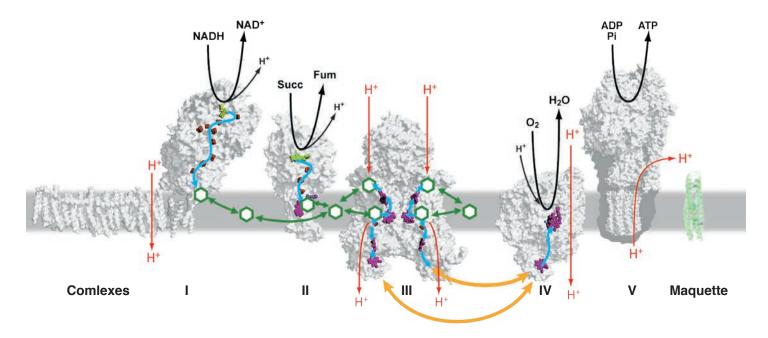


Crossing the Atlantic

How did Dutton, born in England and educated in Wales, make the journey to Philadelphia and Penn? He explains that he did a metabolic project at the University of Wales, "all about oxidation and reduction," and made some discoveries. Wanting to push his work forward, "I thought of the biggest name I could think of" in the area of metabolic pathways. And that was Penn's Britton Chance, Ph.D., D.Sc., then director of what is now called the Johnson Foundation for Molecular

66 Ideas like using man-made proteins to correct genetically inherited diseases in children "are still in the realm of fantasy," said Les Dutton. But he reminded listeners that only 15 years ago, "the very thought of an iPhone would've been considered fantasy."

Biophysics. Dutton wrote to him, and Chance accepted him into the Foundation's program — "which I was amazed about." In fact, Dutton never really worked with Chance: "He let me go off on my own." Some of the other 15 or so postdocs were much less independent. The first eight months in Philadelphia, Dutton continues, "were very tough," for cultural reasons. In addition, when he got his first paper together, Chance was skeptical. As it turned out, however, that paper became the



Art of a different kind is required to illustrate Les Dutton's scientific work. This figure shows the process by which Complexes of mitochondria generate energy from respiration. As electrons (in blue) move through the chains of redox cofactors in each Complex, like hemes (purple), on their way to oxygen, energy is produced that is geared to pump protons (red) across the mitochondrial membrane. When the protons return across the membrane through complex V, they drive ATP formation, the chemical energy molecule that maintains life.

fourth most cited of Dutton's many publications. Still, despite the director's doubts, Chance nevertheless spent the foundation's money for the equipment Dutton needed. As Dutton puts it, Chance was immensely skilled at developing equipment to solve problems.

At that time, the medical school's department, then Biophysics and Physical Biochemistry, was attached to the Johnson Foundation, serving the need to train Ph.D.s. During the Nixon administration, there was a change in the funding mechanism at the National Institutes of Health. "Brit told us all to write grants — and those who got grants became assistant professors!" Dutton was one of them. As he puts it, much too modestly: "I kind of slivered up." Then, when Chance stepped down as director of the foundation, Dutton was appointed to succeed him. "I didn't even imagine that possibility." Years later, in receiving the John Scott Award, Dutton was following Chance in another way: Chance was similarly honored in 1992.

"I feel very lucky to have become a scientist in the Sixties," says Dutton, citing the improved equipment of that time and later advances such as the molecular biology wave of the 1980s and the advent of crystallography in the 1990s.

Every Breath You Take

The Department of Biochemistry and Biophysics, which Dutton led from 1994 to 2008, states its overarching goal this way: "to understand molecular mechanism in medicine and how to exploit this understanding for therapeutic purposes." The particular work by Dutton cited by the Scott Award advisory committee – elucidating "the elementary processes of oxidation-reduction and the diverse biological events coupled to it" – is indeed an understatement, given how central it is.

"Bottom line – over the years, we have described how quantum mechanics is translated to basic biology via natural

selection," he explains. "Every time we breathe, bringing oxygen into our bodies, we activate electron tunneling, which ultimately makes biochemical energy in the form of the molecule ATP. In a way, to put this fundamental knowledge into stark perspective, when humans die, we ultimately die of power failure."

To understand just how basic Dutton's work is, we need to first unpack his nomination citation. *Oxidation-reduction*, or redox for short, is electron transfer, which happens when an electron moves from one molecule to another. Redox is the dual mechanism of *oxidation* – the loss of electrons or an increase in oxidation state by a molecule – and *reduction*, the gain of electrons or a decrease in oxidation state. Many biological processes rely on the biochemical energy produced by electron transfer in redox reactions: for example, photosynthesis, respiration, and detoxification.

As a postdoctoral fellow with Chance (who died in 2010) and since then, Dutton and colleagues have shown how biological electron transfer makes use of the principles of quantum mechanics. In basic terms, within and between proteins, electrons don't hop from redox carrier molecule to molecule; instead, they "tunnel" as a wave through the molecular space in the proteins.

The Transfer of Electrons

In the 1980s, Dutton, with his graduate students at the time, Chris Moser and Marilyn Gunner, applied the Marcus Theory to electron transfer in the early steps of photosynthesis. (Rudolph A. Marcus, Ph.D., from the California Institute of Technology, won the 1992 Nobel Prize in Chemistry for his eponymous theory. In the Nobel press release, it was described as "perhaps the simplest chemical elementary process, the transfer of an electron between two molecules.) No chemical bonds are broken in such a reaction, but changes take place in

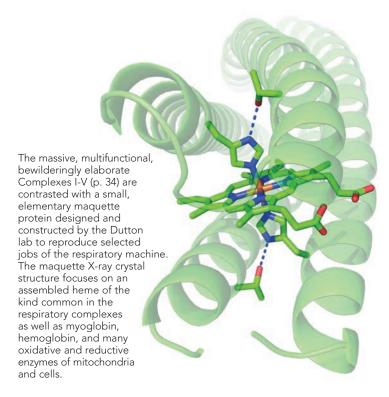
the molecular structure of the reacting molecules and nearby molecules. This shifting of shape enables electrons to move between the molecules. The process was extremely challenging to determine, and Gunner actually measured it for the first time in a natural protein in her Ph.D. thesis.

By the end of the 1980s, Dutton and Moser broadened the picture and demonstrated how biological systems select – in a Darwinian sense – from among quantum mechanical parameters known to be important in electron tunneling. These include how much a molecule is vibrating; the type of medium in which a molecule resides, such as water in the human body; the "driving force" an electron needs to move from one molecule to another; and the distance between the molecules.

As it turns out, natural selection focuses most predominantly on the distance. The Moser-Dutton rule, as it came to be known from a 1999 *Nature* paper, lays the rule out in a simple, elegant equation for calculating the rate of electron tunneling in proteins in different biological systems based on the distance between molecules. It is so simple, says Dutton, "that the calculations can be done in one's head."

The upshot, he says, is "that nature likes a distance of 14 angstroms or less" to maintain working electron transfer rates through chains of redox molecules. (1 millimeter = 10,000,000 angstroms.) And the closer the molecules, the faster the transfer.

"If our electron transfer was switched off, we'd all be dead very quickly," he says. "It's basic and ubiquitous. About 25 percent of the world's enzymes are redox proteins" that promote and control reactions driven by electron transfer.



Magnetism and Proteins

One of these basic reactions is related to magnetism. Many forms of life – from microorganisms to animals – are able to sense the Earth's magnetic field. Certain microorganisms make use of molecules such as magnetite that sense magnetic fields. Birds make use of something more sophisticated to help navigate migration over thousands of miles.

Dutton currently is working with a protein that is equipped with the coenzyme flavin, which acts as a light-activated redox-driven magnetic sensor. He is part of a European Research Council Advanced Grant led by Peter Hore, D. Phil., a chemist at Oxford University, who for some time has been studying the fundamentals of quantum dynamics in molecules that help birds sense and use magnetic fields.

The idea of this grant is not only to learn about bird navigation but also to learn how to harness these minute navigation

66According to Les Dutton, "If our electron transfer was switched off, we'd all be dead very quickly. It's basic and ubiquitous."

devices for something useful to humans. Dutton's job in this collaboration is to design and construct a flavin-based protein with the magnetic properties of a molecular-scale compass.

This is only the most recent direction Dutton's laboratory has explored. He has spent the last two decades building a protein platform for light- and redox-active proteins of many kinds familiar in nature. A paper that brings all of these concepts to fruition appeared in *Nature Chemical Biology* (October 2013).

"We're trying to cash in on the idea that in nature, flavin and other redox molecules such as hemes [as in hemoglobin] or quinones – when wrapped in different proteins – can do many things," explains Dutton. "We show that one protein platform, with a few chemical tweaks here and there, will incorporate many different redox-active molecules. That platform is a basis from which to create many types of electron-transferring enzymes known in nature – but our platform is man-made."

In 2009, Dutton, Moser, and their team suggested that this step might be possible when a forerunner of this platform was transformed into an oxygen transporter – even though its protein structure was unrelated to the iconic structure familiar in the body's oxygen carriers, myoglobin and hemoglobin.

Like Making a Bus

To build their protein, the members of the team started with three amino acids, which code for a helix-shaped column. From this structure, they assembled a four-column bundle with a loop that resembles simple candelabra. They added





Dancers

Les Dutton touches up Alessandra

histidine amino acids to bind the chemically active heme group that contains an iron atom so that it could bind oxygen molecules. They then added another amino acid called glutamate to provide strain to the candelabra; that helped the columns open up to capture the oxygen molecule. Because heme and oxygen degrade in water, the researchers also designed the exteriors of the columns to repel water as a way to protect the oxygen payload inside. The recent Nature Chemical Biology paper shows how to make the "candelabra" do other things with the captured oxygen.

"That exercise was like making a bus," says Dutton. "First you need an engine and we've produced an engine. Now we can add other things on to it. Using the bound oxygen to do chemistry was like adding the wheels."

If you take a look at Dutton's other pursuits – namely his art – it makes sense that he calls the proteins he builds maquettes, a term borrowed from the fine arts and design worlds. Maquette is French for scale model, used to visualize and test ideas without the cost and effort of producing a fullscale piece.

From Lab to Studio

When asked about his art, Dutton hastens to say that, "as a painter, I'm not a commodity by any stretch of the imagination." At the same time, however, he certainly has had his successes. He recalls starting to draw when he was 10 years old or younger, and the results "seemed decent." In his mid-teens, he tried painting and found it something he very much enjoyed doing. In fact, his painting "probably interfered with my work at Penn as a postdoc" - but on the whole it does not seem to have held him back! During those early years in Philadelphia, he would paint in the basement or living room and had a show through the University City Arts League. He's also had a few exhibitions in Cardiff, Wales. One of his more notable sales was a painting of a Liverpool street scene, bought by Lord Snowden, the famous photographer and husband of Princess Margaret.

And for many years, Dutton's caricatures of the faculty members of Biochemistry and Biophysics appeared on the department's home page. Most of the sketches were done at meetings, he explains, and done "surreptitiously." In a few cases, he had to draw from photographs and, he feels, "you can tell the difference." Dutton continues to do sketches,





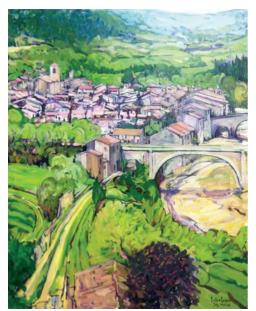
Three sketches of Britton Chance

sometimes in unlikely places. He mentioned sketching both the pianist Lang Lang and the conductor Simon Rattle in concert last year at the Kimmel Center for Performing Arts – done from "miles away." To some extent, Dutton argues, less detail can be better for cartoonists and sketch artists.

In 2001, Dutton bought a house in Lagrasse, a medieval town in the south of France. Among its features, in addition to some stunning natural surroundings, are a Benedictine abbey, founded in 799, and a 12th-century bridge. The French authorities, Dutton notes, keep a close eye on any renovations that would change the village's traditional look. More recently, Dutton also set up a studio in Lagrasse, and that is now where he does most of his painting. When he's in Lagrasse, he goes to the studio twice a day, interrupted by what he calls "a French lunch hour," which may in fact be a tad longer than that. Recent works include a large painting called Après la Cène, a humorous variation on Leonardo's iconic painting of the Last Supper. Dutton's features 13 women, some in modern dress and at least one in no dress at all. The women of Lagrasse who stopped by to view it, he says, approved of the painting and its depiction of "strong women." One of Dutton's friends, Ursula Owen, a feminist activist who co-founded

the Virago Press in London in the early 1970s, recently made a somewhat more ambiguous comment: "There's a great deal going on in the painting and it says a lot about Les's thoughts on women – but I have no idea what those thoughts are."

Another "redo" by Dutton was inspired by Leonardo's *Lady with an Ermine*. Dutton, shown in the photograph at work at his painting, has substituted a baby for the ermine and the lady's hair is now blond. On the other hand, the necklace and the headbands are similar, and the overall resemblance would be obvious to many viewers. Still, it is clearly not a copy. He's also done nudes somewhat in the style of Modigliani, lean and elongated, and has tried his hand with ballet dancers, one of the favorite themes of Degas. Dutton's landscapes, he notes, "are the most original to me," and Lagrasse and its surroundings certainly offer much in the way of inspiration.



Part of Lagrasse Triptych

The Rational and the Irrational

Dutton clearly distinguishes science from art. Science, he says, "is endeavoring to find a truth" and its aim is to be, ultimately, useful. Art, in contrast, can be very interesting and attractive, "but it has nothing to do with the truth." Even more: "science is attempting to approach a rational truth. In art, you can be entirely irrational." The apparent irony, however, is that "I've always done them in parallel." He also reports that he always spends a lot of time thinking about both his science and his art. He is not always sure what he wants to do or where he wants to go. Then, suddenly, "I know what to do experimentally - and start the painting."

In science, there are peer reviews that can provide useful feedback to the scientist. It's not the same in art. When asked how he evaluates his own work, Dutton

replies: "I'm a fretter in terms of asking myself, 'is this good enough?' "Then, he says, "I fiddle at the end." For example, he wonders whether he should touch up the face of the "Lady" who is not holding an ermine, but then one runs the risk of ruining the painting. The artist has to know when to walk away from the project.

When it comes to science, Dutton says, surprisingly, "I'm not a details person." Instead, he tries to do something that no one's done before. "If it's big enough," he explains, "it does not require fretting." With his art, he takes a different approach: "I always try to do something that is more than I can do – and then I do it." As when creating proteins, perhaps?

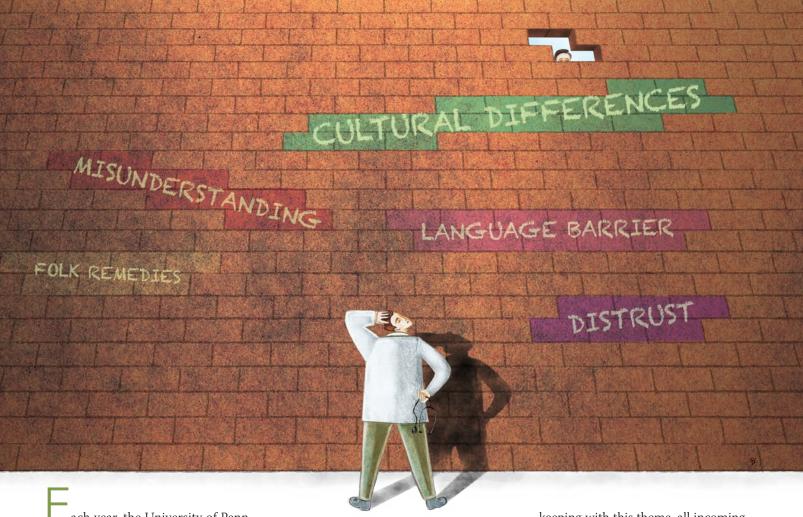
To those who know him, his scientific work, his administrative stints, and his art, Les Dutton has been "doing it" – and doing it very well – for a long time. \Box



Après la Cène

The Role of Culture in Health

By Sally Sapega



ach year, the University of Pennsylvania sponsors a series of events throughout its campus focusing on a central theme chosen by faculty, staff, and students. The topics are broad and multi-layered – some recent themes were Water, Sound, and Proof. For the 2014-2015 academic year, the focal point is another expansive topic, Health.

The Year of Health was chosen, in part, because of the national focus on health-care issues. But closer to campus, the theme also acknowledges and celebrates the upcoming 250th anniversary of the Perelman School of Medicine. In

Penn take Doctoring 1A
(Introduction to Medicine and Society) in their first semester. The course examines the influence of social and cultural forces on doctoring relationships.

keeping with this theme, all incoming first-years students were required to read Anne Fadiman's *The Spirit Catches You and You Fall Down*, as part of the annual Penn Reading Project. The book – which was the focus of a recent University panel discussion – explores the story of the Lees, Hmong refugees from Laos who immigrated to California. Their daughter, Lia, begins to have seizures as an infant. The doctors at the clinic where they bring Lia diagnose her with severe epilepsy. The Hmong know the illness as *quag dab peg* (the spirit catches you and you fall down).

The Lees spoke no English, a significant barrier in and of itself, but, as one physician in the book noted, "The language barrier was the most obvious problem, but not the most important. The biggest problem was the cultural difference."

Indeed, while Lia's physicians tried to treat her with medication, her parents preferred a combination of Western medicine and folk remedies to coax her wandering soul back into her body. Foua, Lia's mother, does not give her prescribed medicine because she does not understand what the doctor has told her, but, even more important, it goes against the Hmong culture of using plants, herbs, and rituals to treat illnesses. As one of the physicians put it, "I felt that I was trying to penetrate a very dense wall — a cultural wall — and didn't have the tools to do it." As a result, despite the best intentions of everyone involved, cultural differences and miscommunication led to tragedy. Lia, who died in 2012, lived the last 26 of her 30 years in a persistent vegetative state.

Cultural differences can make a significant impact on many levels, but especially in medicine; a disconnect between patient and provider can result in poor outcomes. At the panel discussion, Beth Linker, Ph.D., associate professor of history & sociology of science and director of the University's Health and Societies Program, noted that in times of stress, "people retreat to a comfortable place, the center of their own culture. Lia's parents became more Hmong while her doctors became more medical, more rational." Clearly each person's own identity - where we come from - influences how we respond to others and how we look at the world. Although The Spirit Catches You was published 17 years ago, its lessons are enduring: we should not use our cultures to judge others.

Giang Nguyen, M.D., M.P.H., M.S.C.E. '07, assistant professor of family medicine and community health, came to this country from Vietnam with his family in the 1970s. He has found that many immigrants constantly go back and forth between worlds and cultures. He spoke of a relative who has Alzheimer's disease and is in a nursing home. As Nguyen told it, his aunts believe spirits play a role

in the disease. "Does the fact that they believe there might be spirits involved change the fact that my aunt is in a nursing home? No. But if you completely dismiss [the family's beliefs], do you lose a partner in arranging her care?"

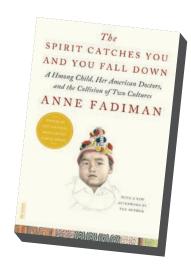
Because Penn Medicine cares for such a diverse population of patients, cultural competency is – and needs to be – an integral part of care. Asking about a patient's cultural and religious beliefs – and their potential impact on care – is a standard part of every initial assessment when a patient is admitted. In the Clinical Practices of the University of Pennsylvania, the ambulatory care component of Penn Medicine, this question is asked of all new patients and of those who have not been seen in more than a year.

A recent article in *Modern Healthcare*, "Language Liabilities," noted that some safety experts are concerned that healthcare providers are not making professional interpreters and translation services

Cultural differences can make a significant impact on many levels, but especially in medicine; a disconnect between patient and provider can result in poor outcomes.

available to patients and families. Instead, they may rely on nonprofessionals who have little knowledge of medical terminology (September 1, 2014). It also cited a study that found that patients whose original languages were not English were significantly more likely to have multiple 30-day readmissions at a Los Angeles hospital.

To overcome such language barriers, all hospitals in Penn's Health System offer translation services around the clock. Its inner-city locations offer access to more than 200 languages, over the phone or in person. A recent *Philadelphia Inquirer*



article noted that in the past seven months alone, patients required interpreters for 52 languages at the Hospital of the University of Pennsylvania.

Being sensitive to language issues is part of cultural competency, to which students at the Perelman School of Medicine are introduced early in their medical careers. Doctoring 1A (Introduction to Medicine and Society), which all students take their first semester, examines the influence of social and cultural forces on doctoring relationships. Subsequent "Doctoring" courses throughout the first three years "revisit various elements of the first course while new ones are introduced," said Horace DeLisser, M.D. '85, G.M.E. '91, an associate professor of medicine who also serves as associate dean for Inclusion and Diversity. "There is a lot of discussion around these issues. Students use their collective experiences to arrive at an understanding."

Medical students can also gain reallife experience by volunteering at one of Penn's many community clinics that serve immigrant, minority, and disadvantaged groups, such as Puentes de Salud or the United Community Clinic.

Overall, the goal is to teach students "ways of engaging with patients and approaching these situations," said DeLisser. "'How do I begin the conversation? How do I ensure we're hearing each other?' We want students to think about these issues and learn."

Launching Our Next



The Countdown Begins

Cake Party Marks 250 Days to Celebration Weekend

Perelman School of Medicine and University faculty and students, the Penn Band, and Ray Perelman welcomed the School's 250th year with a birthday party featuring more than 100 eggs' worth of cake.

In 250 more days, all medical alumni are invited to join the celebrants for reunion weekend.

Highlights of the weekend will be:

The ribbon cutting for the Henry A. Jordan M'62 Medical Education **Center** on May 15, 2015.

The 250th Celebration Gala at the Philadelphia Museum of Art on May 16, 2015. In the meantime, alumni and friends will convene at events across the nation to commemorate the School's significant birthday.

> For 250th Celebration Events, go to the web: www.pennmedicine.org/250th.

Our Origin Story

Dedication to the Best in Medical Research. **Education, and Care**

A graduate of the first class of the University of Pennsylvania, Dr. John Morgan, C 1757, undertook strenuous academic and medical training on his path to founding the first medical school in America.

He served a six-year apprenticeship with Dr. John Redman at Pennsylvania Hospital, beginning in 1751, the year the hospital opened as the colonies' first.

As regimental surgeon in the Pennsylvania militia, Dr. Morgan worked with surgeons trained in Britain, and from 1760 to 1765 he studied at the most advanced medical schools and training institutions in Europe.

He became a member of the Royal College of Physicians of London and a Correspondent in the Academy of Surgeons in Paris. He was one of the first of the Perelman School's professors to earn his M.D. degree at the University of Edinburgh.



Founding professor Dr. John Morgan. A Penn graduate, Dr. Morgan wed Mary Hopkinson, sister of his classmate Francis Hopkinson, who signed the Declaration of Independence.

Dr. Morgan was very aware of the broad significance of founding medical education in America. Upon his return to Pennsylvania, he presented his credentials to the trustees of the College of Philadelphia, Penn's precursor institution. He was made the first Professor of the Theory and Practice of Physic on May 3, 1765.

Dr. Morgan was invited to deliver the commencement address later that month. His text, Discourse Upon the Institution of Medical Schools in America, remains a classic in the history of Amer-

66Your medical school for anatomy and the able professors give advantages not to be found elsewhere. 99

- President Thomas Jefferson

ican medical education and delineated the basic principles that still guide Penn Medicine today:

- Commitment to academic excellence and life within a university, where teaching and learning come first.
- Clinical experience is essential.
- Dedication to science and scientific discovery.

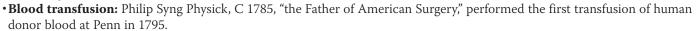
The school achieved national success, drawing students from throughout America.

250 Years

Our Trajectory

Throughout our history, our campus has attracted extraordinary people who have played a part in the development and dissemination of the life-saving advances of American medicine: ending childhood diseases, transplant surgery, curative radiation, medical and surgical treatments for cancer among them.

The Perelman School has been home to extraordinary breakthroughs:



- Philadelphia chromosome: Peter C. Nowell, M.D. '52, G.M.E. '56, Hon '10, and David Hungerford, C '61, discovered the "Philadelphia Chromosome," for the first time linking cancer to a genetic abnormality.
- Cognitive therapy: In 1962, Aaron T. Beck developed cognitive therapy, a pioneering form of psychotherapy focused on the negative "automatic thoughts" that underpin many psychiatric disorders.
- IVF: Luigi Mastroianni, Jr., G'08, the William Goodell Professor of Obstetrics and Gynecology, performed the Greater Philadelphia region's first successful in vitro fertilization in 1983.
- IV feeding: In 1966, Jonathan Rhoads, G.M.E. '40, Hon '60, developed total parenteral nutrition, or IV feeding, following decades of investigation with his mentor I. S. Ravdin, and student Stanley J. Dudrick, M.D. '61, G.M.E. '67.

The School's alumni include accomplished and influential physicians, among them Nobel laureates and other highly regarded researchers, policy makers, and leaders in academic medicine. Our alumni and our faculty are leaders in their communities, who set the standard and the example for the profession across the U.S.



This year, you can show your support for the Perelman School of Medicine through these signature programs:

The 250th Celebration Gala

Philadelphia Museum of Art, May 16, 2015

Purchase a sponsorship, table, an ad in the program book, or tickets and support the 250th Celebration Fund, a term fund for medical education. All ticketholders will be listed in the program book.

The Distinguished Professorship Challenge

Penn Medicine trustee champions George Weiss, W'65, HON'14, and Richard Vague have pledged matching funds to spur the creation of new professorships.

Giving Information

To learn more or to make a gift today, call (215) 898-0578, visit PennMedicine.org/giving, or send your check made out to the "Trustees of the University of Pennsylvania" to:

Penn Medicine Development & Alumni Relations 3535 Market St., Suite 750, Philadelphia, PA 19104-3309

The Henry A. Jordan M'62 **Medical Education Center**

This spectacular new facility will soon become the focal point for the Perelman School.

Join the more than 50 alumni and friends who have named facilities in the Jordan Center. Naming opportunities for the City View Patio and other spaces are still available. Or support the building with a gift to the Henry A. Jordan M'62 Medical Education Center Fund.



What's Your Penn story?

Email us at PennMedicine@alumni.upenn.edu and tell us what brought you to Penn or about a memorable experience related to your Penn years, and we'll be happy to work with you to post it on our 250th blog.

PROGRESS NOTES

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1960s

Robert B. Daroff, M.D. '61, professor and chairman emeritus of the Department of Neurology at Case Western Reserve University School of Medicine, received The Lifetime Achievement Award from the National Headache Foundation at its 2014 annual meeting. He is a former president of both the American Neurological Association and the American Headache Society and former editor in chief of Neurology, the official publication of the American Academy of Neurology. In 2003, Daroff received the Distinguished Graduate Award, the highest honor Penn's School of Medicine gives to alumni. The award booklet described him as "an internationally recognized leader and pioneer in the field of neuro-ophthalmology, a subspecialty of neurology and ophthalmology that deals with disorders of the visual, ocular motor, and papillary systems."

1970s

Kevin H. Mosser, M.D. '79, became president and CEO of WellSpan Health in October 2013. Since his appointment, WellSpan has partnered with Aetna for the national insurer's first accountable care organization in Pennsylvania and announced plans for a \$50 million emergency department to open at York Hospital in 2017.

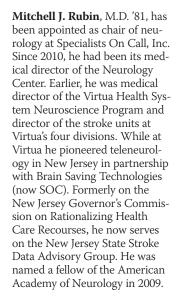
1980s

Ann E. Thompson, M.D., G.M.E. '80, who has been serving as associate dean for faculty affairs at the University of Pittsburgh School of Medicine, will become vice dean of the school on October 1. In her new role,

she will serve as a senior deputy to Arthur S. Levine, M.D., Pitt's senior vice chancellor for the health sciences, in the management and advancement of the medical school. Thompson is professor and vice chair (for professional development) of the Department of Critical Care Medicine and medical director for clinical resource management at Children's Hospital of Pittsburgh of UPMC. She is a former president of the Society of Critical Care Medicine — only the second woman to hold that position -

and serves as a senior editor of *Pediatric Critical Care Medicine*.

Gary W. Dorshimer, M.D. '81, G.M.E. '82, has been named the official physician of the Philly Pops. He is also head team physician for the Philadelphia Flyers and team internist for the Philadelphia Eagles. A clinical associate professor of medicine in the Perelman School of Medicine, he is also section chief of general internal medicine at Pennsylvania Hospital.



Brian A. Hannah, M.D. '84, has joined Mercy Health System as chief medical information officer. He is a practicing physician who was CMIO for Aria Health in Philadelphia. Early in his career, Hannah practiced as an emergency room physician and was a founding member of the Aria Health Hospitalist Group

Jay Allen Barth, M.D. '89, was named chief medical officer of Amicus Therapeutics. He has more than 15 years of experience in drug development, clinical research, and medical affairs. As chief medical officer, he will be responsible for all clinical development activities as well as regulatory affairs. A member of the American Gastroenterological Association, the American College of Gastroenterology, and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition, Barth is also the author of numerous publications in the fields of medicine and clinical research.



William A. Eaton, M.D. '64, Ph.D. '67, received one of this year's Distinguished Graduate Awards from the Perelman School of Medicine. He is an NIH Distinguished Investigator in the National Institute of Diabetes and Digestive and Kidney Diseases, which he joined in 1968 as a medical officer in the U.S. Public Health Service.

Eaton, whose doctorate is in molecular biology, discovered and explained the highly unusual time course and sensitivity of the fiber formation of sickle hemoglobin and showed its role in both the pathophysiology and therapy of sickle cell disease. He has made significant contributions to the field of protein folding by pioneering the application of pulsed lasers to dramatically improve the time resolution in kinetic studies and by developing single-molecule fluorescence methods to watch individual molecules fold and unfold. Eaton

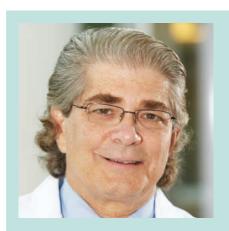
has also developed a mathematical model of protein folding capable of quantitatively explaining a wide range of equilibrium and kinetic experimental results.

Since 1986, Eaton has been chief of the Laboratory of Chemical Physics and scientific director of the Intramural AIDS Targeted Anti-viral Program in the Office of the Director of NIH. The program has contributed to the strong record of NIH scientists in meeting the AIDS crisis, and is now being used as a model for new granting programs within NIH in areas such as bioterrorism and orphan diseases research.

A member of the American Academy of Arts and Sciences and the National Academy of Sciences, Eaton has received several honors, including the Founders Award of the Biophysical Society and the John Scott Award of the City of Philadelphia.

1990s

Julie A. Gubernick, M.D. '90, was appointed chief of the Department of Radiology at Einstein Medical Center Montgomery. She previously served as a staff radiologist at Lehigh Valley Hospital and Muhlenberg Hospital in Allentown. Gubernick is a former president of the Philadelphia Roentgen Ray Society.



Alan J. Wein, M.D. '66, G.M.E. '70, the Founders Professor in Urology and chief of the Division of Urology at the University of Pennsylvania, is the recipient of one of this year's Distinguished Graduate Awards from the Perelman School of Medicine. A founding member of the Society of Urologic Oncology, he directs the Urologic Cancer Program at Penn. Through his leadership, the Division is considered among the nation's leaders and its residency program ranks among the top five in the country. His laboratory is widely recognized for many contributions to the physiology and pharmacology of the lower urinary tract, and Wein is acknowledged for his simplified and now commonly used approach for classifying, evaluating, and managing lower urinary tract dysfunction, including inconti-

nence, the effects of neuromuscular disease, and obstruction.

Among his many honors, Wein has been recognized by the American Urological Association and has received the Urodynamics Society Lifetime Achievement Award and the Ferdinand C. Valentine Award of the New York Academy of Medicine. He was awarded an honorary degree from the University of Patras, Greece. In 2012, he was a recipient of The Edward L. Keyes Medal, presented by the American Association of Genitourinary Surgeons for "outstanding contributions in the advancement of urology." He is the author or coauthor of more than 900 scientific publications or chapters and is editor-in-chief of the gold standard textbook in urology, Campbell-Walsh Urology.

Maryellen E. Gusic, M.D. '90, has been named the chief medical education officer of the Association of American Medical Colleges. Formerly the executive associate dean for educational affairs, the Dolores and John Read Professor of Medical Education, and professor of pediatrics at the Indiana University School of Medicine, she joined the AAMC on October 1.

In her new role, Gusic will examine critical issues in medical education and lead new initiatives to transform current models of

education and workforce preparation, including efforts to advance interprofessional health education and competency-based learning.

At Indiana, she has led the departments of graduate and continuing medical education, medical student affairs and admissions, and education research, as well as the health professions programs, master's program in medical sciences, and library sciences. She was instrumental in creating the IU Center for Interprofessional Health Education

Gusic is president-elect of the Academic Pediatric Association and senior editor of education for *Academic Pediatrics*.

Adam M. Koppel, M.D. '95, was named senior vice president and chief strategy officer for Biogen Idec. He is responsible for corporate strategy and portfolio management. He joined Biogen Idec from Brookside Capital, the public equity affiliate of Bain Capital, where he had been a managing director. Earlier, he was an associate principal of the McKinsey Health Care Practice.

Christopher L. Vojta, M.D. '95, G.M.E. '00, was appointed chief medical officer of Pulse8 Inc. He has held senior positions with UnitedHealth Group, Deloitte Consulting, and Wyeth Pharmaceuticals. In these roles, he successfully launched major product innovations, including Medicare Advantage Chronic Illness Special Needs Plans; ran the medical management practice of Deloitte Consulting; and launched a medical management IT consulting practice.

2000s

Benjamin S. Bleier, M.D. '04, an ear, nose, and throat physician at Massachusetts Eye and Ear Infirmary, has received the institution's 2014 Norman Knight Leadership Development Award for Otolaryngology. The awards recognize future leaders in otolaryngology and ophthalmology, providing financial support for young clinicians during a critical iuncture in their careers. An assistant professor of Otology and Laryngology at Harvard Medical School, Bleier specializes in rhinology and endoscopic skull base surgery.

According to D. Bradley Welling, M.D., Ph.D., the infirmary's chief of otolaryngology, "Through his research efforts, Dr. Bleier is advancing endoscopic surgical techniques, especially in finding ways to deliver drugs to the brain using novel graft techniques in the nose. This innovative work could lead to new drug delivery methods to the central nervous system to treat symptoms of conditions such as Parkinson's disease."



In 2013, Bleier was appointed associate editor of the *American Journal of Rhinology and Allergy*. He has published more than 40 peerreviewed journal articles to date.

Rachel Zuraw, M.B.E. '09, who earned her law degree from the University of Pennsylvania, has joined Hanson Bridgett LLP at its San Francisco office. She is an associate in the firm's Healthcare Litigation Practice Group. She has experience in a wide range of areas, including complex class actions, antitrust, and regulatory anticipation and compliance. Before becoming a practicing attorney, Zuraw was a lecturer on law and medicine at Penn and an adjunct professor of law and bioethics at



the Drexel University Earle Mack School of Law. Among her published articles is an argument against a tax on cosmetic procedures and an analysis of different types of deception that may be involved in research studies.

FACULTY

John D. Cunningham, M.D. See Class of 1951.

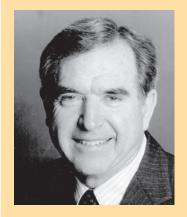
Manucher N. Fallahnejad, M.D. See Class of 1966.

Martin Goldberg, M.D. See Class of 1961.

Martin Helrich, M.D. See Class of 1946.

Donato LaRossa, M.D. See Class of 1971.

J. Donald Ostrow, M.D., Seattle, emeritus professor of gastroenterology at Northwestern University, where he had taught 1978-1995; January 10, 2013. Earlier, he has been professor of medicine and chief of the gastroenterology section in Penn's School of Medicine, 1970-78. He was an expert on bilirubin.



Arnold S. Relman, M.D., the former editor of *The New England Journal of Medicine* who had earlier served as the Frank Wister Thomas Professor of Medicine and Chairman of Penn's Department of Medicine; June 17, 2014. Relman led the department from 1968 to 1977, when he was appointed editor of *NEJM*, professor of medicine at the Harvard Medical School, and senior physician at the Brigham and Women's Hospital in Boston.

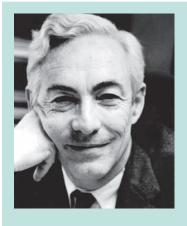
After earning his medical degree from Columbia University, Relman was appointed assistant

professor of medicine at Boston University and remained there until joining Penn. From 1962 to 1967, he was editor of the *Journal of Clinical Investigation*. He was an acclaimed expert in nephrology and electrolyte and acid-base balance.

As his career progressed, however, Relman also became increasingly interested in issues surrounding biomedical research, such as the costs of health care, the role of pharmaceutical companies, and what he saw as the need for universal health-care coverage. Under his editorial direction from 1977 to 1991, the New England Journal increased circulation and influence even as it openly examined economic, ethical, and public policy matters. In 2002, Relman and Marcia Angell, M.D., herself a former editor of NEJM, wrote an article in Daedalus exploring conflicts of interest in the testing and marketing of new drugs. While acknowledging that the missions of drug companies and academic medicine are "in some respects

complementary," they argued that academic medical centers "should avoid financial arrangements that blur the essential distinctions between their separate missions."

Relman was a Fellow of the American Academy of Arts and Sciences and a member of the Institute of Medicine of the National Academy of Sciences. He had also been president of the American Society of Clinical Investigation and other professional associations. A Master of the American College of Physicians, he also received the Distinguished Service Award, presented by the American College of Cardiology, and, from Great Britain, a Fellowship in the Royal College of Physicians in London. Relman held several honorary degrees, including one from the University of Pennsylvania, presented in 1989. The following year, he returned to Penn as part of the 225th Anniversary Celebration of the School of Medicine and was featured in a symposium on the future of health care in America.



Albert J. Stunkard, M.D., emeritus professor of psychiatry and a renowned pioneer in the research and treatment of obesity and eating disorders; July 12, 2014. According to his wife, Margaret S. Maurin, he had worked at his office at Penn until he was 90, two years ago.

In 1955, he published the first description of the night-eating syndrome, a topic he returned to later in his career. In all, he had more than 500 publications - including the book The Pain of Obesity (1980) – exploring the causes and consequences of obesity, while advancing the prevention and treatment of the disorder. Two landmark papers, published in 1986 and 1990, described the significant contribution of genetics to body weight. His studies found that the weights of adoptees showed a far greater resemblance to the weights of their biological parents than to adoptive parents. The work foreshadowed findings that genes explain much of the variation in human body weight. In the headline for its obituary of Stunkard, The New York Times

described him as the "Destigmatizer of Fat"; but it also noted that he "took pains to keep his genetic findings from being seen as an excuse for surrender" (July 21, 2014). Stunkard also was a pioneer in the treatment of obesity, helping to introduce behavior modification techniques and advocating the option of bariatric surgery.

Stunkard earned his medical degree in 1945 from Columbia University. He served two years as an Army physician, principally in Japan, and worked for four years at Cornell Medical College in New York. He joined Penn's Department of Psychiatry in 1957 and was appointed chairman in 1962. He was recruited to Stanford University in 1973 to chair its psychiatry department but returned to Penn four years later.

Stunkard's work was funded continuously for five decades by the National Institutes of Health. He was elected to membership in the Institute of Medicine of the National Academy of Sciences and served as president of several professional associations. He received many awards, including the 1994 Distinguished Service Award from the American Psychiatric Association, the 2004 Sarnat International Prize from the Institute of Medicine, and the 1999 William Osler Patient Oriented Research Award, one of the Perelman School's Awards of Excellence. Penn's Weight Management Program was named in his honor. In addition, he received honorary degrees from Louisiana State University and the University of Edinburgh.

1940s

Henry Parry, M.D. '40, G.M.E. '44, Gwynedd, Pa.; October 4, 2013. In 1958, he helped found Magee Memorial Hospital, the first specialty rehabilitation hospital in the Philadelphia area. He later served as director of rehabilitation in Chestnut Hill.

Rufus C. Goodwin, M.D. '43, G.M.'47, Menlo Park, Calif., a retired ophthalmologist; November 4, 2011.

Walter S. Kerr Jr., M.D. '43, Boothbay Harbor, Maine, emeritus clinical professor of surgery at Harvard University, which has established an endowed chair in his name; March 31, 2013. He had been president of the American Urological Association. During World War II, he served in the U.S. Army.

Harry W. McCurdy, M.D. '43, Bethesda, Md., a retired physician; May 21, 2013. He enlisted in the Army in 1945 and, as a second lieutenant, was in the Philippines when the armistice was declared. He completed his residency in otolaryngology at Geisinger Memorial Hospital in Danville, Pa., before returning with the Army to the Far East and the Korean War. After some years in private practice in the Washington area, he re-enlisted in the Army, serving in, among other posts, Frankfurt, Germany, and Fort Benning, Ga. In 1964 he became chief of otolaryngology at Walter Reed Army Medical Center in Washington, D.C., a position he held until his retirement in 1974. McCurdy played an important role in establishing hearing protection guidelines for the armed services. From 1967 to 1970, he was assistant military attaché at the U.S. Embassy in London. In 1974, he became chief executive officer of the American Council of Otolaryngology.

Martin Helrich, M.D. '46, G.M. '52, Pikesville, Md., emeritus professor and former chair of anesthesiology at the University of

Maryland School of Medicine; June 2, 2013. Previously, he was assistant professor of anesthesiology at Penn. He had served in the U.S. Army.

Robert K. Sassaman, D.D.S., G.M.E. '47, Hellertown, Pa., a retired dentist; March 22, 2013. During World War II, he served in the U.S. Navy.

George W. Hager Jr., M.D., G.M. '48, Haddonfield, N.J., a retired psychiatrist with Cooper Hospital; February 28, 2012. During World War II, he served in the U.S. Army and received the Silver Star, the Bronze Star, and the Purple Heart.

Charles A. Furey Jr., M.D., G.M. '49, Lantana, Fla., retired assistant chief of physical medicine at Thomas Jefferson University Hospital; March 9, 2013. During World War II, he served in the U.S. Army. In order to make money during medical school, he played professional football, earning \$15 per game.

Flora Kaplan Mincer, M.D. '49, New York, retired professor of radiation oncology at the Albert Einstein College of Medicine and Montefiore Hospital; June 20, 2013.

1950s

William S. Wilson, M.D. '50, Bangor, Me., a retired cardiologist; November 8, 2013. He spent two years in the Air Force, then was a professor at the University of Michigan Medical School. In 1967, he was one of the founders of the New Jersey College of Medicine. He also started Northeast Cardiology in Bangor, where he established weekly visits to communities in Eastern Maine to serve patients who needed specialized cardiology care but could not travel.

John D. Cunningham, M.D., G.M. '51, Avalon, N.J., a retired otolaryngologist who had maintained a practice there for many years; July 10, 2013. He had taught at Penn.

Charles A. Skowron, M.D., G.M. '51, Grosse Pointe, Mich., N.H.; March 28, 2013. He began active duty in the U.S. Army Medical Corps in January 1944 and earned a Bronze Star and a Purple Heart. Originally a thoracic surgeon in Boston, he switched to industrial medicine at the Chrysler Corporation in Detroit. After retiring from Chrysler in 1983, he practiced at the Mayberry Clinic.

Henry H. Clapper, M.D., G.M. '52, Naples, Fla., retired surgeon for U.S. Steel and chief of surgery at Timken Mercy Hospital in Canton, Ohio; July 2, 2013.

Walter E. Dandy Jr., M.D., G.M.E. '52, Cockeysville, Md., July 11, 2013. A retired Baltimore anesthesiologist, he helped establish the intensive care unit at Union Memorial Hospital and later served as its medical director. He worked as an anesthesiologist at Johns Hopkins Hospital from 1952 to 1953 before joining Union Memorial. Drafted into the Army in 1953, he was chief of anesthesia and operating rooms at Fort Campbell, Ky., and later at an Army hospital in Munich, Germany. He was discharged in 1955 with the rank of captain. At Union Memorial, he has also served as director of respiratory therapy and medical director of the hospital's dialysis unit.

Samuel J. Friedberg, M.D. '52, San Antonio, a retired physician; October 15, 2013. He served in the Navy in 1954. At Duke University, he was an associate professor of medicine and director of the Cooperative Lipid Laboratory for the Veterans Administration Cooperative Studies in Atherosclerosis. In 1968 he moved to San Antonio, where he was one of the founding faculty members of the University of Texas Health Science Center. He also headed the center's Division of Endocrinology and Metabolism from 1968 to 1975. Friedberg was the author or co-author of more than 40 papers.

John W. Greene Jr., M.D. '52, G.M.E. '56, Lexington, Ky.; November 17, 2013. From 1956 to 1963, he was an assistant professor of obstetrics and gynecology at Penn. He then moved to Lexington to set up research, teaching, and clinical facilities for obstetrics and gynecology at the University of Kentucky Medical School. He led the department as chairman until 1990, but continued teaching medical students. The John W. Greene Society, the department's alumni association, was named in his honor. He published more than 70 scientific papers and five books and served as an examiner for both the American Board of OB/GYN and the National Board of Medical Examiners. He was a trustee of the Frontier Nursing Service and a member of the board of directors of the Planned Parenthood Association of Lexington.

Robert H. Lehner, M.D., G.M. '52, Greendale, Wis., a retired ophthalmologist; October 16, 2011.

R. Wharton Gaul, M.D. '53, Myrtle Beach, S.C., a retired orthopaedic surgeon; November 29, 2013. In 1945, he joined the U.S. Navy as a medical corpsman. He moved to Charlotte in 1957 and helped form a practice that grew to become the Gaul Orthopedic Group.

Robert L. Hall, M.D. '53, State College, Pa., October 11, 2012. An internist, he received the Jane M. Stickler, M.D., Award from the Medical Staff of Mount Nittany Medical Center, presented for "remarkable health-care improvements in Centre County."

Jerel I. Katz, M.D '54, Silver Spring, Md., a retired surgeon; August 5, 2013. He served in the Air Force at Griffith Air Force Base in Rome, N.Y., from 1957 to 1959 and then took a residency at Sinai Hospital. John S. Marshall, M.D. '54, Ligonier, Pa., a retired physician; November 30, 2012. A veteran of the U.S. Navy, he served in World War II. He worked for 40 years in Beaver County and served as chief of staff at The Medical Center, Beaver.

James O'Rourke, M.D., G.M. '54, Farmington, Conn., a retired ophthalmologist and emeritus professor of immunology at the University of Connecticut; Oct. 29, 2011.

David L. Simes, M.D. '54, Ormond Beach, Fla., a retired obstetrician-gynecologist who had maintained a practice there for 30 years; March 1, 2013. From 1955 to 1966, he was an officer in the U.S. Air Force, rising to major. As a flight surgeon and an ob/gyn physician at Maxwell Air Force Base in Montgomery, Ala., he served those stationed at the United States Air War College. In the Daytona Beach medical community, Simes was the first physician to perform a number of now-common procedures, including laparoscopy, and the first obstetrician to invite fathers into the delivery room. Over his long career, he delivered approximately 10,000 babies and assisted countless others in starting families. Simes served as the chief of staff at both Halifax Hospital and Humana Hospital. He was a Fellow of the American College of Surgeons and of the American College of Obstetrics and Gynecology. In addition, he was a Fellow of the Royal Society of Medicine in the United Kingdom and a Life Member of the Medical Society of Vienna. Upon his retirement in 1996, he received a Lifetime Service Award from the Volusia County Medical Society.

Norman B. Ackerman, M.D. '56, Ph.D., New York, N.Y., emeritus professor of surgery at New York Medical College; July 1, 2013. He was the author of *Fat No More: The Answer for the Dangerously Obese* (1999).

William C. Rike Jr., M.D., G.M. '57, San Jose, Calif.; a retired obstetrician-gynecologist; May 19, 2013.

1960s

Claire H. Liachowitz, M.D., G.M. '60, Bala Cynwyd, Pa., former associate professor and chief of physical medicine and rehabilitation at the old Graduate Hospital in Philadelphia; March 15, 2013. Previously, she had been an assistant professor at Temple University Hospital. She was the author of Disability as a Social Construct: Legislative Roots.

Dale S. Penrod, M.D. '60, Philadelphia, a plastic surgeon who had worked at the University of Pennsylvania and Pennsylvania Hospital; May 17, 2013.

Ralph A. Skowron, M.D., G.M. '60, Moultonborough, N.H., retired chief of ophthalmology at West Jersey Hospital in Voorhees, N.J.; January 12, 2013. He had also been chief of ophthalmology at other hospitals. At Kessler Memorial Hospital, he had served as chief of surgery, president of the medical staff, and member of the hospital's board of trustees. He had served as president of the West New Jersey Medical Society. A licensed pilot, he was commissioned in the Air Force. As assistant adjutant general for air, Skowron commanded the Delaware Air National Guard for 12 years.

Spencer Foreman, M.D. '61, Delray Beach, Fla., emeritus president of Montefiore Medical Center in the Bronx; May 28, 2013. Certified in internal medicine and pulmonary disease, he had been president of Sinai Hospital of Baltimore and director of the U.S. Public Health Service Hospital in Baltimore before coming to Montefiore in 1986. Under his direction, the hospital expanded its primary-care network, invested in information technology, and integrated its delivery system, transforming it into a thriving academic medical center. Foreman established innovative social programs to combat HIV/AIDS, tuberculosis, child abuse and neglect, and child lead poisoning. The Children's Hospital at Montefiore opened in 2001. The eight-story Spencer Foreman, M.D., Pavilion, which holds surgical suites, patient rooms, and laboratories, opened in 2006.

Foreman had served as chairman of the Association of American Medical Colleges. In that position, he established an annual award to recognize academic medical centers that go beyond traditional health care to meet the needs of their communities. In 2007, the AAMC renamed the award in his honor. A former chairman of the board of governors of the Greater New York Hospital Association, he had also served on the board of the American Hospital Association (AHA). The AHA presented him with the Justin Ford Kimball Innovators Award, which recognizes individuals who have made outstanding contributions in health-care delivery and financing. He had also been chairman of the board of Ursinus College, where he did his undergraduate education. He was a fellow of the American College of Physicians and a member of the National Academy of Science's Institute of Medicine.

Martin Goldberg, M.D., G.M.E. '61, former professor of medicine in the School of Medicine; June 16, 2013. After completing his fellowship in nephrology at Penn, he was appointed assistant professor of medicine in 1963. He later became chief of HUP's renal electrolyte section and was promoted to full professor in 1970. He resigned from Penn to become chair of the Department of Internal Medicine at the University of Cincinnati Medical Center. From 1986 to 1989, he served as dean of Temple University's School of Medicine. He retired in 1996, but remained active as an attending in nephrology. Goldberg's many honors included the Lindback Award for Distinguished Teaching in 1972 from Penn and the Distinguished Alumnus Award from Temple University's School of Medicine, as well as a Mastership in the American College of Physicians.

Edward D. Johnson, M.D. '61, G.M.E. '65, Chattanooga, Tenn.; October 9, 2013. After working in Atlanta for 20 years, he moved to Sale Creek, Tenn., in 1981, where he opened his own clinic. In 2002, he founded Specialty Medical in Dayton, Tenn., specializing in treating patients with back problems. He retired in 2011.

Gary D. Cody, M.D. '63, Marshfield, Wis., a retired physician; October 22, 2013. He practiced medicine for five years in North Dakota and for more than 29 years in southern Illinois.

Manucher N. Fallahnejad,

M.D., G.M. '66, Gladwyne, Pa., a general, thoracic, and cardiovascular surgeon; July 30, 2013. A fellow of the Philadelphia Academy of Surgery, he was a clinical professor of surgery at Penn and had been associated with Graduate Hospital, the University of Medicine and Dentistry of New Jersey, Main Line Health, and Rowan University.

Donald F. Patterson, M.D., G.M. '67, Seattle, the Charlotte Newton Sheppard Emeritus Professor of Medicine and Medical Genetics in the School of Veterinary Medicine and emeritus professor of human genetics in the Perelman School of Medicine: June 8, 2013. He came to Penn in 1958 as an instructor in the vet school's newly created cardiology section and was appointed associate professor of medicine and medical genetics in 1967 and professor in 1968. Five years later, he was named the first Sheppard Professor; he became emeritus in 1996. Patterson also held many administrative positions, including the first chief of the clinicalcardiology section. From 1985 to 2000, he was principal investigator and director of the Walter Flato Goodman Center for Comparative Medical Genetics, one of the first such centers supported by the N.I.H. He received the American Veterinary Medical Association Lifetime Excellence in Research Award in 2011.

Doris Gorka Bartuska, M.D., G.M.E. '68, Philadelphia, a retired professor of endocrinology and associate dean of curriculum at the Woman's Medical College of Pennsylvania, now the Drexel University College of Medicine; August 4, 2013. She earned her M.D. degree in 1954 from the Woman's Medical College of Pennsylvania. After completing her internship and medical residency, Bartuska received two fellowships from the National Institutes of Health, one in endocrinology at Jefferson Medical College from 1957 to 1958, the other in molecular medicine at HUP from 1966 to 1968. An endocrinologist who advanced treatments focused on the genetic aspects of endocrine diseases, endocrinology of aging, osteoporosis, and thyroid diseases, she also stimulated national interest in a woman's health agenda with emphasis on prevention and treatment of osteoporosis and smoking. Bartuska had been president of the Philadelphia County Medical Society and the Philadelphia Endocrine Society and in 1988 served as president of the American Women's Medical Association. Among her honors was the Strittmatter Award from the Philadelphia County Medical Society, the Distinguished Daughter of Pennsylvania Medal, and the Pennsylvania Medical Society's Distinguished Service Award.

Rolf L. Schapiro, M.D. '69, Pittsburgh, a retired physician; October 12, 2013. At Allegheny General Hospital, he served as chairman of the Department of Diagnostic Radiology for 20 years and was on the hospital's board of directors. Before moving to Pittsburgh, he practiced medicine at the University of Iowa.

Theodore R. Thompson, M.D. '69, New Brighton, Minn., professor of pediatrics at the University of Minnesota; July 28, 2013.

1970s

Donato LaRossa, M.D., G.M.E. '71, Philadelphia, an emeritus professor of surgery in Penn's medical school and HUP surgeon; January 21, 2014. He spent two years, ending in 1976, working at the Army's Fitzsimons Army Medical Center in Denver and was honorably discharged with the rank of major. He specialized in surgery to repair cleft lip and palate defects, as well as reconstructive surgery and aesthetic improvements to the breast, face, and ear. He also operated on melanoma patients. LaRossa was involved in many cleft palate missions in India, Asia, and South America, where he performed many surgeries on needy children. To recognize his longtime commitment to training surgical residents, he received the Penn Plastic Surgery Annual Teaching Award. It was later renamed the Don LaRossa Teaching Award. He also served as director of plastic and reconstructive surgery at the Children's Hospital of Philadelphia. In 2003, he was president of the American Cleft Palate-Craniofacial Association.

James O. Finnegan, M.D., G.M.E. '72, Media, Pa., a retired professor of surgery at Crozer Chester Medical Center; October 13, 2013. He enlisted in the U.S. Navy in 1967 and served as a combat surgeon for the Third Marine Division in Vietnam. He was awarded a Bronze Star and a Purple Heart. A professor of surgery for more than 40 years, he had also been chief of surgery at the Medical College of Pennsylvania and St. Agnes Medical Center. He was the author of In The Company of Marines: A Surgeon Remembers Vietnam (2010).

Pamela M. Foley, M.D. '74, Penngrove, Calif., a retired ER physician; November 8, 2013. She served on the Hope Ship as a part of its medical team. She had also been medical director for the Corte Madera Fire Department's paramedic program and donated her time to Marin Abused Women Services.

Planned Gifts from Drs. Roberts, Franklin, and McCabe Help Augment Class Scholarship Funds

One fundraising priority of our 250th year is to complete as many class scholarship funds as we can. Planned gifts from Brooke Roberts, M.D. '43, Sidney Franklin, M.D. '42, and Edward McCabe, M.D '42, are now kicking in to help meet the challenge.

After dedicating their lives to training generations of medical students, it is only fitting that these three physicians continue to support scholarships through legacy gifts. The gift intent of these donors was either broadly defined or designated for scholarship support; thus, the Perelman School of Medicine can apply them to

a pressing need - maximizing the impact of class scholarship donations and ultimately bringing more of the most talented students to the school.

LEGACY GIVING

Brooke Roberts, a leading vascular surgeon, served for 40 years at the Hospital of the University of Pennsylvania. He helped develop innovative surgical treatments for aneurysms and obstructed arteries, and he advocated



the use of angioplasty as a less-invasive treatment for vascular disease. When he retired in 1983, Dr. Roberts was chief of the Division of Vascular Surgery at HUP and director of the University of Pennsylvania's fellowship in peripheral vascular surgery. His legacy lives on in a surgical lab and endowed professorship named in his honor. The gift toward scholarships from a trust established by Dr. Roberts and his wife, Anna, is one further tribute to his lifelong dedication to medical education.

Sidney N. Franklin was an assistant professor of clinical medicine and attending physician at the Diabetes Clinic at Penn from 1955 to 1982. He was honored by the American Legion in 1977 for his early recognition of Legionnaires' Disease in Philadelphia, saving many lives through his diagnostic acumen. A trust established by Dr. Franklin recently terminated, enabling a gift to be directed to scholarship support at the Perelman School.

Similarly, Dr. Edward McCabe included a gift for the Perelman School in his will. Dr. McCabe worked on the staff of Penn Presbyterian Medical Center for 35 years and served six years as chief of medicine at St. Joseph's Hospital. His bequest will also help provide scholarship support for Perelman School of Medicine students.

The needs for financial support at the School change from year to year, and unrestricted gifts are a great way to ensure that funding will always go to high-priority programs. Gifts like the ones from these physicians were made through a will or trust – the most popular deferred gift received by the Perelman School of Medicine. 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., Executive Director of Planned Giving, at 215-898-9486 or cewan@upenn.edu.

For more information, please visit the website at: www.plannedgiving.med.upenn.edu.

Enthusiasm and Ambivalence

Welcome – some 45 pages later – to the redesigned *Penn Medicine*. Although our designer, Graham Perry of NCS Studios, is the same, he and his colleagues have introduced a new look to our pages. We believe the redesigned issue will serve our mix of interesting and varied content very well.

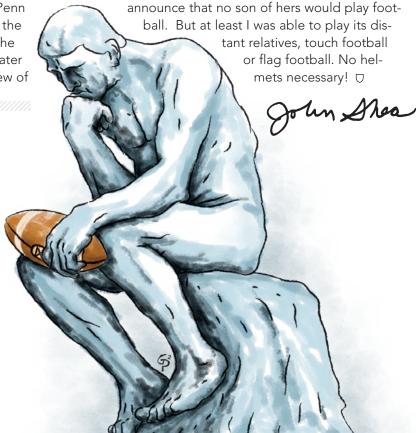
At least one of this issue's features would have been unimaginable when I became editor of this magazine. Imagine, an article on an alumna who . . . blogs? For one thing, blogging was just coming out of its infancy in 1998, and many readers back then would have had a hard time conceiving why a doctor would waste her time that way. But in 2014, Wendy Sue Swanson, M.D. '03, makes a very convincing case that physicians must be aware that their patients are paying attention to social media – and that physicians must be ready to counter the health misinformation their patients may come upon. After all, who is better suited to examine the evidence? So she makes use of the same social media to respond.

The cover story in our redesigned magazine is actually a suite of three articles, "The Brain in Peril." Marshall Ledger, former editor of *Penn Medicine* and a longtime contributor, attended an event earlier this year at the College of Physicians of Philadelphia. He was there to hear three physicians – including two alumni, one of whom is a Penn professor – discuss an increasingly newsworthy topic: the injuries that playing football can cause. In this case, the focus was on chronic traumatic encephalopathy. We later decided to broaden our scope and include an overview of

concussion studies at Penn and a look at a newer concern: the effects of blasts on people in the military. Mark Wolverton, also a frequent contributor, wrote those articles.

Despite the apparent difference in subject matter of "The Brain in Peril" and "The Doctor Prescribes . . . Information," there is at least one intersection. Swanson, in one of her blogs, states unequivocally that she would not allow her sons to play football. That view is shared by the three doctors who spoke at the event at the College of Physicians. But sometimes we sense a certain amount of ambivalence as well. After all, Douglas Swift, M.D. '80, was good enough through high school and college to have played in the National Football League. There remains a certain affection for the game and some of the things that go along with it: teamwork, a common goal, athleticism, and so on. Swift notes that he even enjoyed the hits. So the warnings against playing football do not come without recognition of its attractions.

On a much lower level, I share that ambivalence toward football. I certainly enjoy watching the Philadelphia Eagles play, but I also can't help wincing at some of the collisions and hits, especially when a receiver is, as they say, defenseless. When I was a boy, too, my mother would occasionally





Coming Up: As we approach the Perelman School of Medicine's 250th birthday in May, it's fitting that the Winter 2015 issue of Penn Medicine will include an extensive look back at the school's long and illustrious history.

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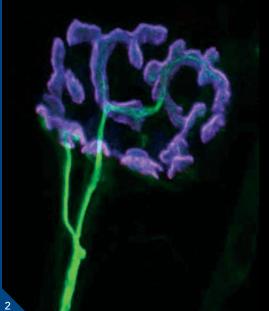


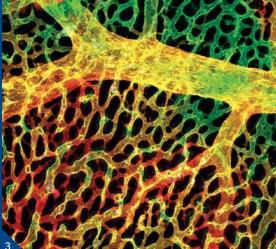
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The Art in Science, the Science in Art

As a recent competition has again demonstrated, art and science are not mutually exclusive. The winning entries of the 2014 "Art in Science" competition are both scientifically instructive and eye-catching.

In the postdoctoral fellow category, the winner is Jessica Talamas, Ph.D. She is a fellow in the laboratory of Maya Capelson, Ph.D, assistant professor of cell and developmental biology. The Talamas image (1) shows the imaginal eye and antennae disc from a fruit fly larva – the immature cell cluster that eventually becomes the adult eye and antennae. The blue is the DNA in cell nuclei and the green is the armadillo protein, part of the wnt/wingless signal pathway.

In the graduate student category, there were two winners. Andrew Moore is a first-year Ph.D. student in the Neuroscience Graduate Group, still doing his lab rotations.

During his stint in the lab of Erika Holzbaur, Ph.D., professor of physiology, he made an image (2) of a neuromuscular junction from the hind leg of a mouse while surveying the muscles of mutant and normal mice. His winning image shows a normal junction – green is the axon connecting, or synapsing, with the purple muscle. Moore will soon choose his Ph.D. project and thesis mentor.

Amanda Phillips-Yzaguirre, a graduate student in the lab of Nancy Speck, Ph.D., professor of cell and developmental biology, is a second-time winner of the competition. Her winning image (3) this year is yolk sac vasculature from a mouse embryo 10 ½ days old. The image is actually a composite of 21 slices, or stacked images, with distinct colors for different layers within the tissue. Overlap between colors results in new colors.



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