



PENN Medicine

SUMMER 2009

THE TRANSFORMATION OF TRANSFUSION MEDICINE

Remembering Bernie Johnson
In the Year of Darwin: How Did
Humans Survive — and Evolve?
A Master of Endoscopy

Keeping Up the Good Work

Last year, when the American Medical Student Association (AMSA) issued its first scorecard evaluating conflict-of-interest policies at American medical colleges and colleges of osteopathic medicine, Penn's school was one of only seven to receive an A. The PharmFree Scorecard assessed the policies in several areas that held the potential for conflict of interest. These included gifts and meals from industry; consulting relationships; disclosure of financial conflicts; pharmaceutical samples; and degree of access that industry sales personnel had to the medical school or hospital.

This June, the association, with the help of the Pew Prescription Project, issued its second scorecard. This time around, it was equally parsimonious with its As. Only nine of the 149 schools (6 percent) received the highest mark, Penn Medicine among them. Thirty-five schools received Fs; 23 of those received the mark because they declined to submit their policies for review. Others received a grade of "In Process" because they were reviewing or revising their policies. The good news, according to AMSA, is that more than one-fifth of U.S. medical schools improved their conflict-of-interest policies in the last year, and the number of perfect scores increased.

A recent study published in *Archives of Internal Medicine* (May 11, 2009) strongly suggests that Penn Medicine's policies have had a noticeable effect on its students. The authors include David T. Grande, M.D., M.P.A., assistant professor of medicine at Penn. The study compared the attitudes of medical students at Penn, which has restrictive policies toward pharmaceutical marketing, with those at the University of Miami School of Medicine, which has

less restrictive policies and permits gifts, meals, and samples from pharmaceutical firms. The researchers sought to test the students' attitudes toward the more expensive cholesterol drug Lipitor and the less expensive drug Zocor. During the testing, some of the students were provided with promotional materials for Lipitor – to measure whether their attitudes toward the drug would be influenced. As the authors report, "Students at Miami responded as we hypothesized, shifting their preferences in the direction of the branding exposure (i.e., Lipitor). However, students at Penn had a boomerang response, i.e., a behavioral response opposite of the implied marketing intent." One explanation the authors suggest is Penn's "strong school policy." The policy, that is, that earned the school an A from AMSA.

The computations made for the PharmFree Scorecard seem simple compared to those involved in determining what could be called the "power rankings" in Alzheimer's disease research. Three of Penn Medicine's leading investigators are featured in this issue's "What's New in Alzheimer's Research?" (pp. 20-21). They also appear in a recent article in the *Journal of Alzheimer's Disease*, "Alzheimer's Disease Research: Scientific Productivity and Impact of the Top 100 Investigators in the Field" (March 2009). Aaron A. Sorensen, of Collexis Holdings, Inc., has crunched the numbers, making use of the "author-disambiguation algorithm," the "scientometric viewpoint,"



and an investigator's "H-Rank-minus-SeTH-Rank disparity as well as its polarity." Based on papers published between January 1, 1985, and April 21, 2008, Sorensen has produced three lists of researchers.

Among the most prolific investigators, Virginia Lee, Ph.D., M.B.A., director of Penn's Center for Neurodegenerative Disease Research, and John Q. Trojanowski, M.D., Ph.D., director of Penn's Institute on Aging and director of the Alzheimer's Disease Center, are ranked together at 10th. Gerard D. Schellenberg, Ph.D., a recent recruit to the Department of Pathology and Laboratory Medicine, is ranked 89th. In addition, Murray Grossman, M.D., Ed.D., professor of neurology at Penn, is ranked 98th.

Lee is 8th among most-cited authors and Trojanowski 10th. They reappear among the authors with highest H-indices, which measure the overall impact of an investigator: Lee is 3rd and Trojanowski 4th. Schellenberg is ranked in the middle of both lists.

Sorensen also considered the impact of the two major research awards in the field, the MetLife Alzheimer Award and the Potamkin Prize. He notes as well which investigators have been elected to the Institute of Medicine of the National Academy of Sciences. Lee and Trojanowski have won both awards and are members of the Institute. Schellenberg has received both awards.

Current faculty members are not the only ones with strong Penn connections to make the power rankings. Allen D. Roses, M.D. '67, G.M.E. '71, of Duke University, was the first investigator to identify a susceptibility gene for late-onset AD, apolipoprotein E. Not surprisingly, he is ranked 3rd among "Most Cited." He is also named as 30th among "Most Prolific" and 26th among authors with the highest overall impact. ▀



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TRANSFUSION MEDICINE: TRANSFORMED, TRANSLATIONAL, AND PERSONALIZED *By Thomas W. Durso*

Penn's Division of Transfusion Medicine has moved far beyond the traditional roles of pathology and laboratory medicine, maintaining its diagnostic function but developing therapeutic roles as well. For example, researchers can now use the standard blood-banking processes to collect and purify lymphocytes that can be re-engineered to combat specific infections or attack cancer cells.

REMEMBERING BERNIE JOHNSON *By Sally Sapega*

Bernett "Bernie" Johnson Jr., M.D., one of the most respected and beloved figures on the Penn Medicine campus, died in April. Chief medical officer of HUP, he was also a professor of dermatology, an award-winning educator, a champion of community service, and a painter.

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TWO DAYS IN THE YEAR OF EVOLUTION

By Martha Ledger

As part of Philadelphia's year-long celebration of Charles Darwin and his epochal theory of evolution, the University Museum of Archaeology and Anthropology hosted a two-day colloquium that featured researchers in anthropology, biology, and biomedicine. Experts from the School of Medicine made significant contributions to the colloquium and to the museum's exhibition.

A PERSONALIZED VACCINE HELPS FIGHT RECURRENCE

By Rabiya Tuma and Holly Auer

Follicular lymphoma is a disease that frequently recurs and eventually becomes resistant to available therapies. Now, idiotype vaccines, made from the tumor cells of patients with follicular lymphoma, can boost the length of disease-free survival by 44 percent.

WHAT'S NEW IN ALZHEIMER'S RESEARCH?

For the Penn Medicine faculty members who investigate Alzheimer's disease, 2009 so far has been a year of advances, some major funding, and recognition beyond the usual academic and research spheres. That recognition comes in part from two independently produced documentaries that feature several Penn professors.

GREGORY GINSBERG, MASTER OF ENDOSCOPY

By Dawn Fallik

Director of endoscopy for Penn's Health System, Gregory Ginsberg, M.D., has built a national reputation as an innovator in interventional endoscopy and diagnosis. He is also known for his work in trans-endoscopic surgery, a new field in which surgeons operate through natural openings in the body.

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Thompson

A “Dream Team” Is Ready to Tackle Pancreatic Cancer

Craig B. Thompson, M.D. '77, the professor of medicine who serves as director of Penn's Abramson Cancer Center, has been selected to lead what the sponsoring organization is calling a research “Dream Team.” Daniel D. Von Hoff, M.D., senior investigator and physician-in-chief at the Translational Genomics Research Institute in Arizona, is the other leader. Principals on the team are drawn from Johns Hopkins University School of Medicine, Princeton University, and the Salk Institute for Biological Studies. With \$18 million in funding from Stand Up to Cancer, Thompson's team is poised to lead the nation's most innovative research project on pancreatic cancer. In particular, the researchers hope to learn more about what metabolic nutrients pancreatic tumors rely on to grow; the goal is that, with that knowledge, scientists will be able to develop new therapies designed to cut off those nutrients. Pancreatic cancer is the fourth-leading cause of cancer deaths in the United States; more than 90 percent of patients die within the first year of diagnosis.

Stand Up to Cancer is a charitable initiative of the Entertainment Industry Foundation. In May, Stand Up to Cancer awarded the first round of three-year grants to five multi-disciplinary and multi-institutional teams. Most of the funding was raised in connection with a telecast the initiative sponsored on September 5, 2008, aired simultaneously on ABC, CBS, and NBC. In all, the foundation awarded \$73.6 million among the five research teams.

According to Sherry Lansing, chair of the board of the Entertainment Industry Foundation, “Stand Up to Cancer grew from two simple constructs: scientists need more money for research and easier ways to work together; and the entertainment industry has unique resources that can be called upon to help make every American aware that each and every one of us has a role to play in advancing cancer research.” Lansing is a former CEO of Paramount Pictures.

Recent studies have demonstrated that most cancer cells acquire mutations that cause them to become addicted to a continual supply of nutrients to produce the energy they need to survive and proliferate. In most cancers, this nutrient is glucose. Pancreatic cancer presents a unique challenge because it is addicted not to glucose but to another molecule, glutamine. When cancer feeds or metabolizes excess amounts of glutamine, it can lead to extreme weight loss by robbing other cells of this important nutrient, a condition from which many pancreatic cancer patients suffer. Cancers that use excess glutamine are often resistant to standard forms of chemotherapy, another characteristic of pancreatic cancer. The goal of Thompson's research team is to understand the “fuel supply” of pancreatic cancer, which would help scientists develop more individualized treatments with fewer side effects.

Acknowledging Excellence

The Hospital of the University of Pennsylvania has continued its rise in the annual ranking of hospitals by *U.S. News & World Report* (August 2009). Again this year, HUP earned a spot on the magazine's “Honor Roll,” reserved for the hospitals that receive high rankings in at least six of the 16 specialty categories. HUP is ranked 8th, up from 10th last year and 12th in 2007. More than 4,800 hospitals were evaluated, and only 21 made the “Honor Roll.”

In all, HUP is ranked in the top 50 in 15 specialties, improving its position in nine and holding its position in one. The specialties ranked in the top 10 are: Digestive Disorders; Ear, Nose, and Throat; Diabetes & Endocrine Disorders; Heart; and Respiratory Disorders. In the top 20 are: Geriatrics; Gynecology; Kidney Disease; Urology; Psychiatry; and Rheumatology.

Pennsylvania Hospital, one of Penn Medicine's three hospitals, was ranked in the top 50 in two specialties, in Neurology & Neurosurgery and in Orthopaedics.

Since 1990, *U.S. News & World Report* has provided a ranking of hospitals' quality of care on a nationwide basis. The magazine evaluates hospitals on mortality rates, technology, staffing of nurses, and factors related to the individual specialties, as well as reputation among a group of randomly selected board-certified physicians

Grant to Study Esophageal Cancer Is Renewed

The National Cancer Institute has renewed a Program Project at Penn, granting investigators at the School of Medicine \$7.5 million over the next five years to support research on new ways to treat esophageal cancer.

“This new award builds upon the multi-disciplinary effort conducted by

an outstanding team of investigators at Penn and other institutions,” says Anil K. Rustgi, M.D., the T. Grier Miller Professor of Medicine and Genetics and chief of the Gastroenterology Division. As Rustgi, the overall principal investigator on the grant, points out, “There has been significant progress in this cancer that historically has been very difficult to diagnose and treat.”

Continued research on esophageal cancer is critical for prolonging patient survival, especially because this type of cancer becomes prevalent in its later stages and patients often have a poor prognosis and a reduced response to traditional chemoradiation therapy. This research will build upon the investigators’ previous findings, which made substantial progress in deciphering the molecular and cellular biology that underlies esophageal cancer. In addition, their findings are expected to have broad applications to other related cancers in the lung, head and neck areas, and skin.

One project will focus on the biological roles of oncogenes (EGFR, c-Met) and tumor suppressor genes (p53, p120catenin) in esophageal carcinogenesis, as well as the mechanisms by which tumor cells invade healthy tissue (Rustgi). Other projects will deal with how blood vessels and fibroblasts interact to allow tumors to invade (Meenhard Herlyn, D.V.M., Sc.D., a professor of dermatology at the Wistar Institute and an investigator in Penn’s Institute for Translational Medicine and Therapeutics), and how the protein cyclin D1 is regulated in the nucleus and in the cytoplasm (J. Alan Diehl, Ph.D., associate professor of cancer biology and director of cancer cell biology at Penn’s Abramson Family Cancer Research Institute). The projects are unified further by core facilities at Penn, and collaborators come from the Dana Farber Cancer Institute/Broad Institute in Boston and Massachusetts General Hospital.

How Do Heart Muscle Cells Develop?

Researchers at the School of Medicine will receive \$2 million over the next four years from the American Heart Association and the Jon Holden DeHaan Foundation to study how the regeneration of heart muscle cells can help improve outcomes for cardiac patients. This award establishes an American Heart Association-Jon Holden DeHaan Foundation Cardiac Myogenesis Research Center at Penn, led by Jonathan Epstein, M.D., chair of the Department of Cell and Developmental Biology. The sponsors also funded two centers at other institutions.

In particular, the researchers aim to determine how these cells develop and to better

understand their inner molecular workings. Their hope is that findings from this research will lead to new ways to treat heart attacks, congenital heart disease, and heart failure.

The Penn Heart and Vascular Center Opens

The construction of the Ruth and Raymond Perelman Center for Advanced Medicine has provided the opportunity to consolidate several cardiovascular practices and streamline the experiences of outpatients. The Penn Heart and Vascular Center opened recently on the second floor of the Perelman Center’s East Pavilion.

Combining heart and vascular practices from throughout Penn’s Health System, this multi-disciplinary model



Celebrating a Class’s Achievements

The 151 members of the Class of 2009 received their diplomas and recited the Hippocratic Oath for the first time as doctors on May 18, at Philadelphia’s Kimmel Center. This year’s Graduation Speaker was Christine K. Cassel, M.D., president and CEO of the American Board of Inter-

nal Medicine and the ABIM Foundation. She is a leading expert in geriatric medicine, medical ethics, and quality of care. In the photo, Daniel del Portal, M.D., who delivered remarks on behalf of the Class of 2009, receives congratulations from Arthur H. Rubenstein, M.B.,B.Ch., dean of the School of Medicine and executive vice president of the University of Pennsylvania for the Health System.

shifts the focus from individual practices to specific diseases. The center combines not only cardiologists, cardiac surgeons, and specialists in vascular medicine but also nurse practitioners, physician's assistants, nurses, social services, and administrative support staff from all practices.

"With providers from every type of heart and vascular specialty in one place, we are able to develop a plan of care, whether it requires eventual intervention, surgery, or just medication," said Michael A. Acker, M.D., the William Maul Measey Professor of Surgery and chief of the Division of Cardiovascular Surgery.

The center's staff in a central check-in area welcomes all patients. Similar providers – such as vascular surgery and vascular medicine – are physically adjacent to each other, making the transition from one appointment to the next easy for patients.

Noninvasive heart and vascular imaging is located one floor below. The center also offers an expanded capacity for outpatient echo and vascular testing capacity. Pre-operative testing and imaging have been reorganized so that patients can have all tests performed during one outpatient visit to prevent frequent return visits for the patients.

Honors & Awards

Jill M. Baren, M.D., M.B.E., associate professor of emergency medicine and of pediatrics, has become president of the Society for Academic Emergency Medicine, the nation's largest organization devoted to research and education in the specialty. Baren, an expert in emergency care, the subspecialty of pediatric emergency medicine, and medical ethics, will lead 5,000 national and international members of the society. Among issues Baren will address during her yearlong tenure are the potential effects of a regionalized emergency care system modeled after the one that delivers trauma patients to hospi-



Baren

tals that meet specific care benchmarks.

Before coming to Penn in 1997, Baren served on the faculty of the Yale University School of Medicine and taught at U.C.L.A. School of Medicine, where she completed her emergency medicine and pediatric emergency medicine training. She also holds a master's degree in bioethics from the University of Pennsylvania and has lectured and written on informed consent in emergency medicine research and bioethical issues in resuscitation.

Clyde F. Barker, M.D., G.M.E. '59, the Donald Guthrie Professor of Surgery and former chair of the Department of Surgery, received the Lifetime Achievement Award at the Annual Meeting of the Society of University Surgeons. The award recognizes individuals who have had a sustained career in academic surgery with contributions to the surgical sciences and who have demonstrated a commitment to the Society. Barker also received the Thomas E. Starzl Prize in Transplantation and Immunology, presented by The University of Pittsburgh School of Medicine, the Department of Surgery, and the Thomas E. Starzl Transplantation Institute. The award honors Barker's "outstanding clinical and scientific achievements." Both awards cite Barker's launching of the clinical transplantation program at the University of Pennsylvania in 1966, when he performed the first kidney transplant in the Philadelphia area, and his work in mak-

ing it one of the largest and most successful programs of its kind.

Ben E. Black, Ph.D., assistant professor of biochemistry and biophysics, has received a 2009 Rita Allen Foundation Scholar Award. The award is made to investigators at leading medical research institutions in the early stage of their careers who show promise of becoming leaders in the fields of neuroscience or immunology, and in the cure and treatment of cancer, cerebral palsy, and multiple sclerosis. Black's laboratory is interested in how particular proteins direct accurate chromosome segregation at mitosis. He was recognized by the Foundation for his project "Exploring and Exploiting Epigenetic Centromere Mechanisms for Establishing Chromosome Stability." Since 1976, the Foundation has typically made between two and six Scholar Awards each year.

Robert H. Debbs, D.O., clinical associate professor of obstetrics and gynecology and director of the Maternal-Fetal Medicine Network at Pennsylvania Hospital, was inducted as president of the American College of Osteopathic Obstetricians and Gynecologists at its annual conference in March.

David F. Dinges, Ph.D., professor of Psychology in Psychiatry and chief of the Division of Sleep and Chronobiology, received the 2009 Raymond F. Long-acre Award, sponsored by PricewaterhouseCoopers LLC, at the 80th Annual Scientific Meeting of the Aerospace Medical Association in May. He was honored for his significant contributions to aviation safety through the development of the Psychomotor Vigilance Task (PVT), which has become the standard for assessing the effects of sleep loss and fatigue on human performance. The data provided by the PVT has been used to develop models to improve work schedules in aviation, space, the trans-

portation industry, and other shift-working occupations. Dinges's laboratory is unique in its capability to conduct prolonged study of healthy humans in conditions that mimic challenging real-world scenarios.

Dinges is also director of the Unit for Experimental Psychiatry in the Department of Psychiatry and associate director of Penn's Center for Sleep and Respiratory Neurobiology.

James A. Hoxie, M.D. '76, professor of medicine in the Hematology/Oncology Division and director of the Penn Center for AIDS Research, was named a Fellow of the American Academy of Microbiology. The honor is bestowed in recognition of a record of scientific achievement and original contributions that have advanced the field of microbiology. According to the academy, Hoxie has helped to define HIV/SIV envelope interactions with the cell that are critical for entry, that contribute to pathogenesis and immune evasion, and that are targets for therapeutic and vaccine strategies. He has also developed innovative approaches and numerous reagents that are generously provided and widely used.

Marshal Joffe, Ph.D., associate professor of biostatistics and senior scholar in the Center for Clinical Epidemiology and Biostatistics, was elected a Fellow of the American Statistical Association. He was cited for his outstanding contributions to the development of statistical methods and concepts for causal inference. Some of his methodological interests include confounding by variables affected by treatment, the effects of noncompliance, dealing with unmeasured confounders, and observational assessment of screening efficacy.

Jonni S. Moore, Ph.D., professor of pathology and laboratory medicine, was the recipient of the 2008 FOCUS Award for the Advancement of Women in Medicine in recognition of her extraor-

dinary advocacy on behalf of women and junior faculty at Penn Medicine and across the University at large. She has shared her academic advice and her strategies for balancing home and work life. At present, she is chair of the Medical Faculty Senate Steering Committee and a member of the Gender Equity Executive Council. An internationally renowned scientist in the field of cytomics, Moore has developed the largest and most comprehensive academic flow cytometry research laboratory in the United States.

Sylvia E. Rosas, M.D., M.S.C.E. '03, assistant professor of medicine, received the Leadership Fellow of the Year Award from the National Hispanic Medical Association. The organization seeks to improve the health of Hispanics and other underserved populations. Rosas, who is in the Renal-Electrolyte and Hyperten-



Rosas

sion Division, studies the role of novel risk factors in the development and progression of cardiovascular disease in patients with chronic kidney disease. Oxidative stress, inflammation, and lipid metabolism are of particular interest.

Duke Surgeon Named Penn Chair of Orthopaedic Surgery

L. Scott Levin, M.D., has been named chair of the Department of Orthopaedic Surgery, effective on July 1. He is board-certified in orthopaedic surgery and in



Levin

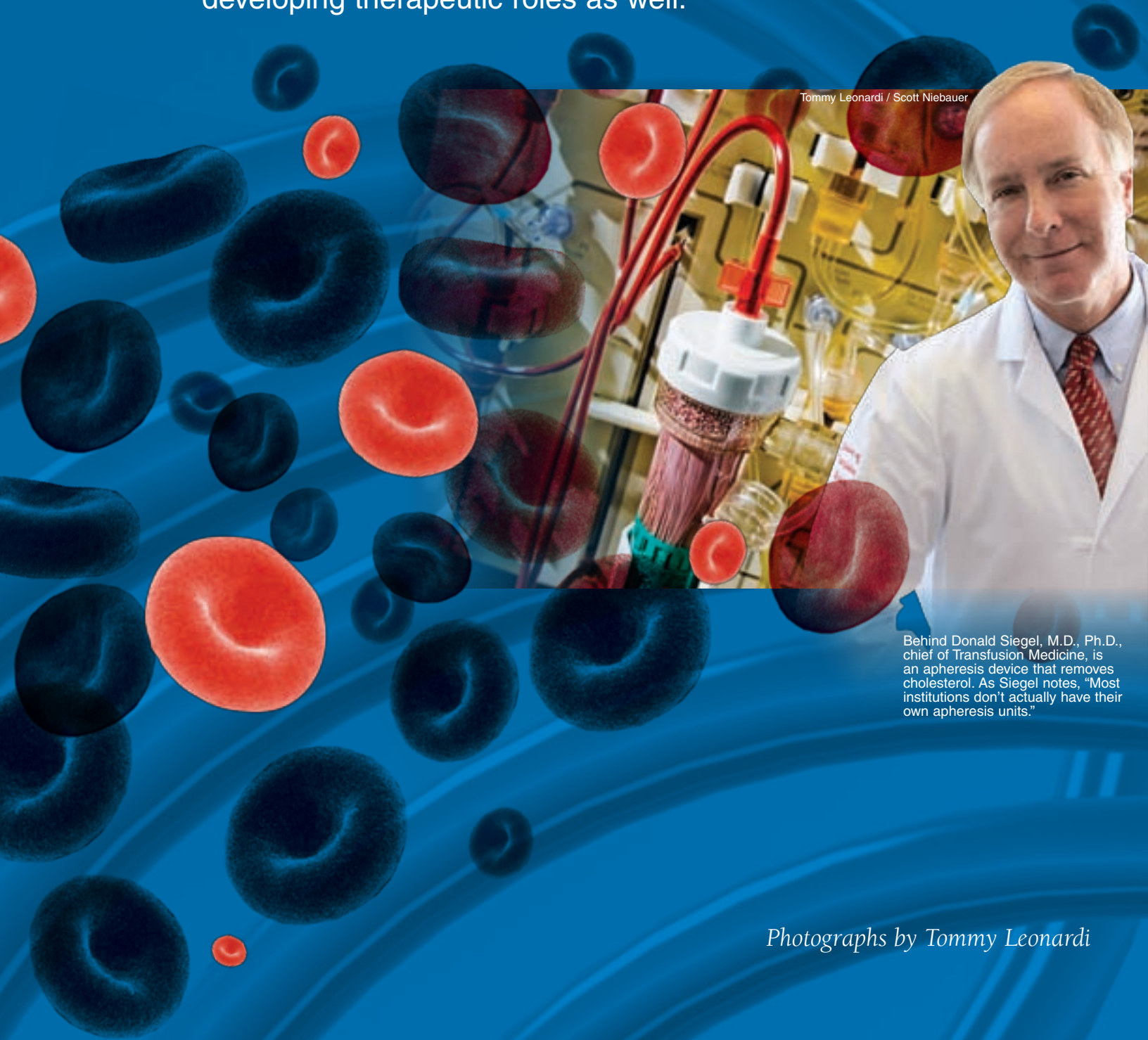
plastic and reconstructive surgery. Most recently professor of both orthopaedic surgery and plastic surgery at Duke University School of Medicine, he served as chief of the Division of Plastic, Maxillofacial, and Oral Surgery. His expertise focuses on surgery of the hand and upper extremity, reconstructive microsurgical techniques for extremity reconstruction, and limb salvage. His primary research interests are extremity soft tissue reconstruction and composite tissue allotransplantation. At Duke, he established the Human Tissue Laboratory and was director of the laboratory and of the Anatomic Gifts Program. Levin has been recognized for his commitment to teaching and won the 2007 Master Clinician/Teacher Award for his accomplishments in both clinical care and education.

Levin is widely published, with more than 170 peer-reviewed journal articles, 60 book chapters, and six books. He has served as chairman of the Advisory Council for Orthopaedic Surgery of the American College of Surgeons, as secretary general of the World Society of Reconstructive Microsurgery, and as president of the American Society for Reconstructive Microsurgery. He is president-elect of the American Society for Reconstructive Transplantation and a member of the board of directors of the American Board of Plastic Surgery. ■

Transfusion Medicine:

Penn's Division of Transfusion Medicine has moved far beyond the traditional roles of pathology and laboratory medicine, maintaining its diagnostic function but developing therapeutic roles as well.

Tommy Leonardi / Scott Niebauer



Behind Donald Siegel, M.D., Ph.D., chief of Transfusion Medicine, is an apheresis device that removes cholesterol. As Siegel notes, "Most institutions don't actually have their own apheresis units."

Photographs by Tommy Leonardi

Transformed, Translational, and Personalized

By Thomas W. Durso

In the late 1980s, as a Ph.D. student at Johns Hopkins University, Bruce Levine (C '84) worked in a bone marrow transplant laboratory. To reach the lab, he had to walk past patient wards, so every day he was directly exposed to the sobering presence of very sick people who were desperately counting on biomedical science – on the kind of work he was doing – to alleviate their suffering.

“That drove home to me why I was doing this research – what effect it could have,” he recalls.

Levine went on to earn his doctorate in immunology and infectious diseases in 1992 and hook up with a researcher named Carl H. June, M.D., for a post-doctoral fellowship at the Naval Medical Research Institute. The two began a cell therapy trial for HIV that yielded increases in CD4+ T cell counts and improvements in immune function. The results led them to conclude that their work had applications beyond AIDS.

Today, Levine and June are at Penn Medicine, in the Department of Pathology and Laboratory Medicine. Levine is a research associate professor and director of the Clinical Cell and Vaccine Production Facility. June is a professor and director of translational research for Penn's Abramson Family Cancer Research Institute. They have continued to culture lymphocytes, leading to the development of several current Phase I clinical trials of adoptive immunotherapy for infection and several types of cancer.

“Many cancer patients who get intensive chemotherapy and stem cell transplants need some supplemental treatment, not only to get rid of potential residual disease but also to more rapidly reconstitute the immune system,” says Levine. “You can give people stem cells, but it takes weeks for some cells to come back, and the lymphocytes take months to years to come back. This is a way of supplementing chemotherapy and stem cell transplantation, and our work has also



branched out to include endowing cells with novel functions to redirect them to kill tumor cells by putting a kind of chimeric receptor on their surface.”

Levine and June are part of the department’s division of transfusion medicine, a group of researchers and clinicians who use techniques associated with blood banking, apheresis, and infusion to treat patients diagnosed with a variety of hematopoietic, immunologic, oncologic, and genetic disorders.

“Many other places have facilities that are very expansive, but the scope and sophistication of what takes place is limited because they don’t have the critical mass of people that Penn has,” says Don L. Siegel, M.D. ’87, Ph.D., professor of pathology and laboratory medicine, chief of the transfusion medicine division, and medical director of the cell vaccine production facility. (He is also vice chair of the department.) “You need individuals with different strengths and backgrounds. You need infectious disease people who deal with HIV and AIDS, you need molecular biologists, you need cell engineers, you need a facility, you need this, you need that.”

Staffed with *this* and equipped with *that*, this division at Penn is spearheading a biomedical revolution and ushering in a new, paradigm-shifting era of personalized medicine. As Siegel remarks, “Personalized medicine is more than just calling your patients by their first names.”

* * *

Traditionally, a department of pathology and laboratory medicine has served a diagnostic function: for more than a century, such departments handled blood tests, biopsies, toxicology screens, and the like, allowing a physician to diagnose a patient’s condition and recommend therapies and treatment. These departments will continue to function as diagnostic agents as the 21st century pro-

gresses, but more and more, according to Siegel, they also will take on therapeutic roles. The development of increasingly specific therapies – operating at the cellular and molecular levels, targeting particular conditions, and with far fewer side effects – holds stunning promise, but because of the complexities involved and the specializations that are necessary, it will be limited to laboratories with certain core competencies.

The range of competencies, Siegel believes, are founded in transfusion medicine.

“The people who run those kinds of laboratories are going to have to do this work in a way that’s compliant with strict FDA regulations and follow the standards set by a number of cellular therapy accrediting organizations,” he says. “That’s what we already do in transfusion medicine. The pathology departments are ready by virtue of being the place where blood banks, transfusion services, and apheresis units are located.”

The notion of such a therapeutic role is a natural extension of the decades-long practice of blood banks: collecting blood, running it through a centrifuge to separate out discrete components, filtering out undesirable contaminants, testing it for infectious disease, packaging it, storing it, matching it to its intended recipient, and preparing it for transfusion at the bedside.

“Conventionally, the cells removed from a blood donor would be transfused back to a patient unmodified in any way,” says Mark L. Tykocinski, M.D., who stepped down last year as chair of Penn’s Department of Pathology and Laboratory Medicine to become dean of Jefferson Medical College and senior vice president of Thomas Jefferson University. “Alternatively, you could take cells, engineer them with some enhanced property, and then put them back into a patient. You could engineer, for instance, immune cells in ways that would make them recognize and attack cancer more effectively than



Donald Siegel confers with Bruce Levine, Ph.D., director of the

pharmacological agents can do, and then put them back into a patient. You can genetically modify the cells by introducing new genes or knocking out those that are there, which in transfusion therapy are things that are best done by highly regulated pathology department laboratories.”

Siegel places these developments within the context of the pharmaceutical industry’s practice of building upon existing therapies to create new ones. “It’s only natural,” he says, for researchers to take standard blood banking processes – the removal of whole blood and fractionation into red cells, platelets, and plasma – and apply them to the collection and purification of other types of circulating blood cells such as lymphocytes that can be re-engineered to combat specific infections or attack cancer cells.

“You might add a gene to the cells you’ve removed to endow them with unique properties, and then expand their numbers in the lab prior to transfusion,” he says. “It makes sense that you’re going to have the same kind of people who are already experienced with the preparation of conventional blood components doing it with other cells.” That, he suggests, is the rationale for pathology departments to provide such therapeutics.



Clinical Cell and Vaccine Production Facility.

The field holds tremendous promise, as therapies in general move away from one-size-fits-all treatment models toward approaches that are more specific to patients and conditions. Chemotherapy, for example, kills rapidly dividing cells – not only cancer cells but also those in the gastrointestinal tract and elsewhere. The goal of the new research is to develop treatments that destroy the cancer while leaving healthy cells alone.

As Tykocinski explains, many of today's modern therapeutics "are not the traditional pharmaceutical small-molecular compounds, but what are called biologicals, generally genetically engineered protein therapeutics, cellular therapeutics, and gene therapeutics."

* * *

Last fall, Penn Medicine opened a newly renovated state-of-the-art blood bank in the transfusion medicine division. Along with a blood donor center slated to open this Fall, these facilities will give the Hospital of the University of Pennsylvania access to blood products without being totally dependent on the local American Red Cross division that experiences frequent blood shortages. In addition to collecting whole blood that

will be fractionated into red blood cells and plasma, the blood donor facility will collect components by an automated process called apheresis that replenishes fluid during the collection process, thus allowing greater numbers of cells to be safely removed from a given donor at one time. This method is particularly valuable for the collection of platelets that are greatly needed by oncology patients at Penn Medicine whose own cell counts have fallen as a unfortunate side-effect of the treatments they are undergoing.

Apheresis devices are used by Penn physicians in the division of transfusion medicine for therapeutic purposes as well. For example, they might be treating a newly diagnosed leukemia patient, who is experiencing such a significant increase in the production of white blood cells that his blood has become dangerously viscous; that condition can lead to stroke-like symptoms. Although chemotherapy will be given to control the disease and, it is hoped, put the patient into remission, apheresis is used in the acute setting to remove the excess white cells and to lower the blood viscosity over a period of a couple of hours.

Such therapeutic apheresis is also used to remove low-density cholesterol. In fact, Penn has the largest group of patients in the country being treated for familial hypercholesterolemia using a unique type of apheresis device that removes LDL-cholesterol but leaves HDL-cholesterol alone. Patients with cholesterol levels that can be as high as a 1000 and who have not responded to Lipitor and similar medications are now coming to Penn every two weeks or so and undergoing a lipopheresis procedure to filter out excess LDLs.

"We're very fortunate to have our own apheresis facility here at HUP," Siegel points out. "Most institutions don't actually have their own apheresis units, and they must rely on outside contractors such as the American Red Cross to come

into their hospitals to perform the procedures at great expense and inconvenience to patients and staff."

In addition to performing apheresis, the physicians in Penn's transfusion medicine division also provide infusional therapies of intravenous medications. Such treatments range from iron for anemic patients to recombinant monoclonal antibodies for those with rheumatoid arthritis, inflammatory bowel disease, and multiple sclerosis. For many patients who need more specific therapies than existing treatments can provide, the new pathway for treatment delivery is a boon. Other conditions Penn doctors are treating in this way include neurological autoimmune diseases, organ rejection, metabolic storage diseases such as Gaucher's, Fabry's, and Pompe's, and immune deficiency disease.

Perhaps one of the most promising avenues being utilized by the transfusion medicine division is in the field of hematopoietic (adult) stem cells. Trans-

Transfusion Medicine in a Nutshell

The Division of Transfusion Medicine, which serves as the therapeutic arm of the Department of Pathology and Laboratory Medicine, comprises the blood bank and transfusion service at the Hospital of the University of Pennsylvania; an immunohematology reference laboratory; an apheresis/infusion unit; a blood donor center; a hematopoietic stem cell collection and processing laboratory; and the Clinical Cell and Vaccine Production Facility. Its clinical services provide more than 80,000 units of blood and blood products per year to HUP patients through the blood bank and transfusion service while performing more than 4,000 procedures in the apheresis/infusion unit on outpatients and inpatients diagnosed with a variety of hematopoietic, immunologic, oncologic, and genetic disorders.



Joanna Sowinska, a blood bank technologist, checks the packets in the HUP Blood Bank with Donald Siegel.

fusion medicine approaches allow for far less intrusive collection of cells and delivery of treatments. For example, the donation of bone marrow, which through conventional means involves the uncomfortable removal of cells from the pelvic bone, can be accomplished peripherally through apheresis. Blood stem cells leave the marrow and circulate in the bloodstream, from which they can be removed, separated out, and either donated to a patient who needs them or returned to the donor at a later time after the donor has undergone some form of treatment.

The division's Clinical Cell and Vaccine Production Facility, which first opened in BRB2/3 in 1999 and moved to an expanded clean room suite in HUP in 2005, has greatly helped Penn scientists who are engaged in translational research – research that Siegel expects will lead to new standards of care. In a paper published last year in *Nature Biotechnology*, Penn researchers and colleagues from Sangamo Biosciences in Richmond, Calif., reported pre-clinical data for a potential new treatment for HIV that reduced the viral load of HIV in mice. The strategy was developed from two separate areas of research. First, the discovery in the 1990s that about 1 percent of Caucasians are highly resistant to HIV infection because they are born with a mutation on a gene called CCR5, which encodes a co-receptor needed by most strains of HIV to


infect CD4+ T cells. Separately, Sangamo developed the technology to exploit the ability of “zinc fingers,” naturally occurring proteins, to specifically bind to DNA. When zinc finger proteins are linked to a bacterial endonuclease enzyme that can cleave DNA, specific genes can be targeted for genetic repair or disruption. “By inducing mutations in the CCR5 gene using zinc finger proteins, we’ve reduced the expression of CCR5 surface proteins on T cells, which is necessary for the AIDS virus to enter these immune system cells,” explains Elena Perez, M.D., Ph.D., currently an assistant professor of pediatrics at the University of South Florida and first author on the study. She performed the research as a postdoctoral fellow in the lab of Carl June, who is senior author of the study. The next step was to adapt the treatment for humans, and this was performed by Levine’s group in the cell production facility. A clinical trial recently approved by the FDA is now recruiting HIV+ patients who are screened prior to having their T cells collected in the transfusion medicine division’s apheresis unit. Those cells are then sent to the production facility to be transfected with genes that encode the zinc finger nuclease proteins to bind to the CCR5 gene and induce mutations in the same spot as the naturally occurring mutation; the process renders the cells unable to produce CCR5 – and thus resistant to HIV.

“The goal is to do this to some cells, and then grow those cells in the lab and put them back into the HIV+ patient,” Siegel says. Toxicity would be minimal because the patient is receiving his own cells, albeit modified to resemble those in the one percent of Caucasians who are naturally negative for CCR5. The hope is that these HIV-resistant cells will then have a survival advantage and proliferate in the body.

Siegel offers another example: a blood cancer patient who comes to the apheresis unit every day for four or five straight days so that his blood stem cells can be collected. The cells go to the division’s hematopoietic stem cell lab, where they are quality-controlled and frozen. Weeks later, when anti-cancer chemotherapy has as an unwanted side-effect that critically weakens the patient’s immunity, a stem cell lab technician comes to the patient’s room with a container of liquid nitrogen holding bags filled with the blood stem cells. The technician thaws the bags one by one at the patient’s bedside in a water bath at body temperature, then transfuses the cells back into his body, where they home in to his bone marrow in order to reconstitute his immune system.

“There’s a lot of discussion about translational research,” Siegel says. “It’s a really big buzzword when they talk about going from bench to bedside. Really, what most people mean by bedside is the bed in a clinical research unit, with all its elaborate monitoring systems and clinical protocols. The *real* translation is when it becomes a routine thing on a regular hospital ward.”

He sweeps his arm back and forth to indicate the place in which he is speaking. “This is just a regular patient room,” he emphasizes. “Ten years ago, this used to be a big deal, but with our colleagues in the hematology/oncology division, hundreds of these procedures are performed per year. (That division is led by Edward Stadtmauer, M.D. ’83.) In terms of transfusion medicine, these



types of activities stretch way beyond the traditional red cell, platelet, and plasma components to the actual creation of new kinds of cellular therapies.”

* * *

In addition to its clinical and research missions, the transfusion medicine division has a strong educational component as well. Through a combined clinical/research fellowship accredited by the Accreditation Council for Graduate Medical Education and supported by an NIH training grant for which Siegel is the principal investigator, Penn Medicine is training a new generation of “personal cell therapists” who it hopes will take the lead in tomorrow’s development of personalized medicine. Elena Perez who had led the HIV study described above, is one of the program’s recent graduates.

It is not a surprising facet of the division, given the integrated, results-oriented way it has approached its charge.

“There are universities and medical centers where there are a lot of politics

and infighting and little silos, and here it’s been completely the opposite,” Levine says. “Among everyone that we’ve reached out to and the people who have come to us, there’s been an immense amount of not only collegiality but also insistence on cooperation and collaboration. That has made these types of trials possible. It’s not just the techniques and the scientists and the facilities here.” He even cites the regulatory support they receive. In all, he says, it’s a combination “that very, very few medical centers around the country or around the world have.”

And to hear Siegel and Levine tell it, that combination of expertise and temperament has helped Penn to build a division that stands poised to do truly groundbreaking work.

“When you talk about personalized medicine, you’re talking about developing a therapy that is incredibly effective and has very few side effects,” Siegel says. “It’s sort of custom-tailored for that particular patient. The form that that kind of therapy takes for treating cancer

or HIV or something like that typically is at the cellular level; it’s not in some chemical in a bottle that you just buy and inject intravenously.”

In other words, researchers are trying, in essence, to teach a person’s immune system to respond to and treat the cancer she has – and *only* that cancer. Under ordinary circumstances, certain cells in the body can recognize rapid cellular division and shut it down before tumors form; cancer somehow fools these detectors into ignoring the signs. By removing the cells from the patient’s body and exposing them to her own tumor antigens in the laboratory, Penn Medicine physician scientists such as oncology surgeons Brian Czerniecki, M.D., Ph.D., and George Coukos, M.D., Ph.D., G.M.E. ’97, G.M.E. ’00, hope to activate native immune mechanisms in the cases of breast cancer and ovarian cancer, respectively. When re-infused back into the patient from which they had been obtained, these cells can serve as cellular vaccines that instruct other cells of the immune system how to recognize her tumor.

“There’s nothing more personal than that when you’re talking about personalized medicine,” Siegel points out.

“There’s really nothing more personal than using your own cells and your own cancer, and creating a vaccine that is sent back into you to destroy your cancer.” It is also a type of therapy for which there can not be competition from large pharmaceutical companies; simply put, they do not have access to the patients to obtain the raw materials and in any case the costs would be prohibitive for them to manufacture anything other than the one-size-fits-all generic drug. “As an added bonus,” Siegel notes, “cellular therapies such as those we already employ as well as those in the future are and will be substantially less expensive than conventional therapies – and should prove much more effective.” ♥

The Chairman’s View

The Division of Transfusion Medicine is one of six divisions within the Department of Pathology and Laboratory Medicine. According to John E. Tomaszewski, M.D., professor and interim chair of the department, “Ours is one of the elite, fully integrated departments of pathology in the country, bringing together the full gamut of clinical services and research interests.” The other divisions are Anatomic Pathology, Neuropathology, Laboratory Medicine, Pediatric Pathology, and Experimental Pathology & Immunobiology. With about 100 full-time members of the faculty, the department is perennially one of the leading recipients of funding from the National Institutes of Health among peer programs. “Leveraging the hospitals and outreach network of the University of

Pennsylvania Health System, our department showcases broad-ranging clinical subspecialty expertise which encompasses forefront diagnostic test development and infusional therapeutics innovation. Our research programs feature dynamic and interdisciplinary interplay between basic and translational research, with consistent funding success.” In particular, says Tomaszewski, “We are positioning our transfusion medicine services to help introduce and innovate a growing armamentarium of biologics (cellular, protein, and gene therapies).” In more general terms, the interim chairman is optimistic: “The early 21st century is ushering in a revolution in diagnostics and therapeutics, and pathology departments will be key drivers for paradigm-shifting in both.”



Remembering

Walking through the hospital or across campus with Bennett “Bernie” Johnson Jr., M.D., was never a quick trip.

“Bernie and I would eat lunch in the doctors’ dining room, but we had to allot an extra 15 minutes to walk from Maloney to 3 Founders,” recalled John Seykora, M.D., assistant professor of dermatology. “He would be stopping, shaking hands with people, hugging them, telling stories. It was always an entourage.”

Johnson, who died on April 3 at the age of 76, was indeed one of the most respected and beloved physician-educators and leaders at HUP and the School of Medicine. He was known as a caring physician with his patients. That trait was especially important when treating patients with vitiligo, a pigmentary disorder that can be extremely disfiguring.

A professor of dermatology who was HUP’s senior medical officer, Johnson took pleasure in teaching both residents and medical students. “They really loved him and felt comfortable with him,” said John Stanley, M.D., chair of the Department of Dermatology. “Students flocked to him in clinics. They all wanted to be with him.”

Johnson’s knack for teaching did not go unnoticed. In 1997, he won the University’s Lindback Award for Distinguished Teaching; ten years later, he received the Walter R. Nickel Award, the highest teaching award given by the American Society of Dermopathology. The Dermatology residents recently announced the creation of the Dr. Bennett Johnson Award for Teaching, to be given to the faculty member who residents feel has contributed the most to their education in a caring and professional manner.

Johnson’s education of medical students went beyond clinical knowledge. “He reminded them that global health is important, but ‘You can see the same disparities here in West Philadelphia,’” said Jack Lewis, director of the School of Medicine’s Office of Diversity and Community Outreach. “He encouraged them to get involved in the community. ‘Your skills are needed here.’”

According to Lewis, Johnson hosted a luncheon every year for incoming students of color, just to check in and see how everything was going. Johnson,

who was also the school’s senior associate dean for diversity and community outreach, “was a great example for students,” Lewis said. He told them, “Be an administrator but also show your human side. Stay in touch with people.”

A very effective advocate for giving back to the community, Johnson worked for 10 years to establish a flourishing collaboration between Penn and Sayre High School in West Philadelphia. Today the Sayre Health Center offers comprehensive health-care services to both students and community members as well as providing health and professional education for students from both the high school and the University. At its grand opening in 2007, Amy Gutmann, Ph.D., president of the University, acknowledged Johnson’s vision. “He is not afraid to roll up his sleeves,” she said. “He is an inspiration to us all.”

Johnson also played a crucial role in Penn’s summer mentorship program. As Lewis describes it, the mentorship program focuses on “middle-of-the-road high-school students who are unsure about continuing their education.” Each year, Johnson met with the high-school

students who had some interest in medicine and health. At the end of the each year's session, Johnson arranged a white coat ceremony for the students, similar to that of the medical students. "The program has turned some of their lives around," Lewis said. "Many went on to attend college."

Johnson was also known for his artistic skills. He began painting when he was a resident and continued throughout his life. He always brought his

told him that I thought it was beautiful. The next day he brought in a print of the painting. "This is all you're getting."

Johnson's dry sense of humor was legendary. "It wasn't always what he said, but his mannerisms," said Garry Scheib, HUP's executive director. "He had a twinkle in his eye, a mischievous smile, and a great laugh. He enjoyed tweaking people."

His wit was evident when he initiated a toll for people crossing in front of his office. "He'd come out and not let you

I asked, the answer was, 'Ask Bernie.'"

Scheib also learned the value of Johnson's knowledge – and composure. "He was always so grounded, he never got flustered," said Scheib. "He'd always keep things simple – get to the root of the issue and deal with it."

In 2005, Johnson won the Edward S. Cooper Humanitarian Award, which recognizes people at HUP who best exemplify a caring, selfless spirit. At the award ceremony, Scheib said, "Bernie represents

Bernie Johnson

By Sally Sapega

camera with him, no matter where he went, and he drew from the photos he took. Throughout the years, his work has been shown on campus through the Faculty Club and the annual Gracie Mansion Art Exhibit in New York City. He won first prize at an art show sponsored by the American Medical Association and a "Best of Show" from the American Academy of Dermatology.

Although Johnson was willing to "share" his paintings, he rarely gave them up. "They were his babies," said Phyllis Murry, an executive secretary in HUP Administration, "One time he did a beautiful picture of a Japanese garden, and I

pass till you paid up the quarter," said Dorothy Horne of Administration. He gave his collected tolls to Diane Corrigan, HUP's chief financial officer, saying they were "to help balance HUP's budget."

Arthur Rubenstein, M.B.,B.Ch., executive vice president of the University of Pennsylvania for the Health System and dean of the School of Medicine, first met Johnson when he came to Penn eight years ago. "Bernie was one of the first people to welcome me. After the usual polite conversation, he let me know that HUP was his hospital . . . and I came to learn that this was indeed quite true. Over the years, no matter what question

the heart and soul of HUP." And its conscience, too, Scheib later added: "He always reminded us of why we are here." ♥

Memorial gifts can be made to Meharry Medical College, Development Office, 1005 Dr. D. B. Todd Jr. Boulevard, Nashville, TN 37208, or to the Bernett L. Johnson Jr. Sayre Health Center Memorial Fund, payable to the Trustees of the University of Pennsylvania, 3535 Market Street, Suite 750, Philadelphia, PA 19104.



CAREER IN A CAPSULE

A native of Richmond, Virginia, Bennett Johnson Jr., M.D., earned his medical degree at Meharry Medical College in Nashville, Tennessee, in 1957. Part of his training in dermatology took place at Philadelphia's Naval Hospital and the Graduate School of Medicine of the University of Pennsylvania. After retiring from

the U.S. Navy Medical Corps, he came to Philadelphia's Graduate Hospital in 1980 as associate chair of dermatology and became a clinical professor at Penn. In 1984, he joined the standing faculty as associate professor. Among his many administrative roles, he had been senior associate dean for veteran's affairs. A fellow of the American Academy of Dermatology, he was one of the editors of an edition of a classic

textbook in his field, *Lever's Histopathology of the Skin*. He was named Practitioner of the Year by the National Medical Association in 1993 and served on the National Board of Medical Examiners.

Two Days in the Year of EVOLUTION

By Martha Ledger

In celebrating the synthesizing genius of Charles Darwin, researchers in anthropology, biology, and biomedicine provided a thought-provoking picture of who we humans are.

I think
D
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Then between A & B. various
types of relation. C & B. The
first predation. B & D
rather greater distinction
than former would be
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February 12, the 200th anniversary of Darwin's birthday, was unseasonably warm in Philadelphia. Diagonally across from the University Museum of Archaeology and Anthropology, the site of the day's celebration, a man in a mustard-colored winter jacket spoke through a bullhorn to no one in particular. He rotated right and left, sending his voice by turns into 33rd Street, then Spruce Street. ". . . Jesus loves the . . . knows every hair on . . . take Him into . . ." Is he there every day, I wondered? Or did he come on purpose to remind the Darwin celebrants that not everybody believes in evolution?

Inside the domed cavern of the museum's Harrison Auditorium, it's likely that everybody, religious or not, did believe in evolution. They had come for a two-day colloquium that would illustrate and celebrate Darwin's influence on 21st-century biological and biomedical research. Twelve scientists had been invited to present their research. Each one eminent in a different niche, they all dealt with some aspect of variation – the essence of the evolutionary process.

The colloquium was conceived by the School of Medicine's Howard Goldfine, Ph.D., professor of microbiology, and Michael Weisberg, Ph.D., assistant professor of philosophy in the School of Arts and Sciences, chairs of Penn's Year of Evolution. The audience was largely University faculty, students, and staff, but the event was also open to the public.

For scientists, evolution is a done deal. When I interviewed him, Goldfine reminded me of the famous 1973 pronouncement by geneticist and evolutionary biologist Theodore Dobzhansky: "Nothing in biology makes sense except in the light of evolution." The sequencing of human and other genomes continues to validate Darwin's theory. Homologous genes have now joined homologous organs and skeletal parts as proof of common ancestry. Darwin's concept of natural selection as the primary mechanism propelling change is similarly accepted.

The paleontological record also supports Darwin's theory, and that was laid out two floors above Harrison Auditorium in an ambitious, interactive exhibition called "Surviving: The Body of Evidence." (Supported by a National Science Foundation grant and many donors, the \$2.4-million exhibition remained at the University Museum until May, then went on tour to a series of other museums.) The curators – Alan E. Mann, Ph.D., emeritus professor of anthropology at Penn and now professor of anthropology at Princeton University, and Janet M. Monge, Ph.D. associate professor of anthropology at Penn – use epoxy casts of some of the world's most famous fossils to trace the multi-million-year emergence of humans as upright creatures with large brains. The exhibition's evidence of our divergence from apes includes a cast of the 3.7-million-year-old footprints of bipedal hominids discovered in Tanzania by Mary Leakey as well as a succession of skulls with progressively larger craniums and smaller jaws.

Despite overwhelming evidence of evolution, not everyone is on board with the theory. The 2005 decision in *Kitzmiller v. the Dover [Pennsylvania] School Board* – that intelligent design is not science and doesn't belong in a science curriculum – did not deter similar curricular challenges in other states, nor the open-

ing in 2007 of the \$27-million Creation Museum in Petersburg, Kentucky, which displays life-size dinosaurs coexisting with humans in the Garden of Eden. The museum had half a million visitors in its first nine months.

Two Americas exist around the issue of evolution, according to Kenneth R. Miller, Ph.D., the colloquium's keynote speaker, who addressed this reality before an audience that fully packed Harrison Auditorium. Miller, a professor of biology at Brown University, referred to the 2007 Gallup poll showing that only 49 percent of Americans believe in naturalistic evolution and noted that, among countries in the developed world, only Turkey had a lower percentage.

People fear evolution for a variety of reasons, he explained. For one, it makes humans the product of chance. Also, it contains no moral imperatives, and people fear that society could easily implode without such guiding constructs.

Miller, who was the prosecution's main witness in *Kitzmiller* and is author of the most widely used high-school biology textbook in America, offered his own favorite evidence for evolution: It's based on the fact that chimpanzees and other apes have two chromosomes more than humans do. Because the loss of two chromosomes would have been fatal for humans, he said, scientists hypothesized that some distant eon ago, two pairs of chromosomes must have gotten stuck together and fused. So they looked for chromosomes with extra telomeres (sequences that cap the ends of chromosomes) and an extra centromere (a DNA region that's located in the middle of a chromosome). What they found was that human chromosome 2 has an extra centromere and internal telomere sequences. Its genes correspond almost exactly to chimpanzee chromosomes 12 and 13.

"Evolution is the only way to explain these facts," he said.



Photo by Candace diCarlo

Janet M. Monge, Ph.D., one of the curators of the University Museum's exhibition on evolution, "Surviving: The Body of Evidence," contemplates a fellow mammal.

SARAH TISHKOFF: TRACKING HUMAN DIVERSITY

The biologists at the colloquium the next day painted a rich and complex portrait of Darwin. He emerged not only as the genius who laid out the theory of evolution and natural selection, but also as a model scientist. He published six books on botany and four volumes on marine biology. “He was not a mere theorizer,” asserted Paul D. Sniegowski, Ph.D., associate professor of biology at Penn. “He carried out the difficult and humble work of observing and experimenting, and he submitted his work to his peers for criticism.” *The Origin of Species* was Darwin’s most influential work, but it was only one among 19 books he wrote.

Good as he was, Darwin never figured out how the variations arose that natural selection acts upon. That was done by Gregor Mendel. We know now that variations arise through the reshuffling of genes during reproduction, as well as from errors in genetic copying. Recent comparisons of genomes have uncovered evidence of another source of variations — the frequent transfer of genetic material across species, mostly by viruses that cut and paste DNA from one genome to another. At the colloquium, two scientists talked about yet other variation-generating mechanisms that go beyond the traditional paradigm.

Susan L. Lindquist, Ph.D., a member of the Whitehead Institute and professor of biology at the Massachusetts Institute of Technology, studies the folding and misfolding of proteins, among which are prions. Prions are proteins that fold themselves into unusual shapes and cause other proteins to do the same in a kind of disastrous chain reaction. (Stanley B. Prusiner, M.D. ’68, received the 1997 Nobel Prize in Physiology or Medicine, as the Nobel press release put it, “for his pioneering discovery of an entirely new genre of disease-causing agents” — prions.) A prion is implicated in mad cow disease (Creutzfeldt-Jakob disease). Lindquist and

When it comes to DNA, humans are pretty much the same. What interests Sarah A. Tishkoff, Ph.D., is the one-tenth-of-one-percent difference from person to person.

Tishkoff is the David and Lyn Silfen University Associate Professor of Genetics and Biology and one of ten Penn Integrates Knowledge professors who have appointments in two of the University’s schools. In her case, they are the School of Medicine and the School of Arts and Sciences.

She studies genetic variations in African populations and has done extensive fieldwork in Africa, sometimes in remote areas. With her collaborators, she has amassed the world’s largest DNA database from more than 7,000 blood samples given by individuals from more than 100 African ethnic groups. “Africans, previously, had been underrepresented in studies of human diversity,” she said at the Darwin colloquium at Penn’s University Museum of Archeology and Anthropology.

Tishkoff is looking for genetic variations that predispose Africans — and African-Americans — to certain diseases, such as hypertension and diabetes. She’s also investigating variations in drug-metabolizing genes so that treatments for these diseases and HIV infections can be targeted more effectively. As she put it, “The goal is better health care for Africans.”

During the Darwin celebration, Tishkoff found herself simultaneously at two com-

memorative sites: the colloquium and the exhibition “Surviving: The Body of Evidence,” where she appears in a film about recent and future human evolution.

In the film, she describes a genetic variation associated with malaria, a disease that kills one million people annually and affects five million at any one time. The variation gives some Africans living in malaria-ridden areas a bit of protection against the disease. They can still get it, but will be less seriously ill. Because malaria arose just five or six thousand years ago, the origin of the survival-enhancing genetic variation occurred fairly recently — sometime less than 300 generations ago.

If the variation definitively supported survival, it would probably be more widespread than it is. “It’s a mixed blessing,” Tishkoff explained during a recent phone conversation. It’s linked to a deficiency in the enzyme G6PD, which can lead to life-threatening anemia when triggered by certain foods and drugs. Ironically, some of the drugs used to prevent malaria are triggers in people who have this deficiency.

At the colloquium, Tishkoff, who in 2003 was named one of *Popular Science* magazine’s “brilliant 10” American scientists, reported on lactase persistence as another beneficial genetic variation that was conserved. The enzyme lactase is produced by epithelial cells in the small intestine, and it enables newborns to digest milk.

her colleagues discovered, however, that, in fungi, some prion chains can lead to beneficial traits. They now think that such chains may actually help maintain stable synapses in higher organisms. The newly configured protein moves directly from one generation to the next, wholly out-

side the normal path of DNA replication, making it a plausible vehicle for the rapid evolution of new traits.

In another study, Lindquist and her colleagues showed that overstressing heat-shock proteins (specifically Hsp90) leads to the expression of new traits as well.



Photo by Tommy Leonard

Lactase production generally shuts down as children become adults. But not in all cases. Humans with a certain genetic variation continue to produce enough lactase to digest dairy products into adulthood. Northern Europeans, especially Scandinavians, have this trait in abundance; there's somewhat less lactase persistence in central Europe and almost none in Africa.

Tishkoff, however, found lactase persistence in contemporary East Africans who have descended from pastoralist tribes. Archaeological data show that cattle were first domesticated in East Africa around 5,000 to 5,500 years ago. Through computer simulations based on the number of genetic recombinations that have occurred in the region of the lactase mutation, Tishkoff was able to date the African genetic variation to roughly that same time. The cultural and genetic events seem to have co-occurred: the domestication of cattle created an environment that was favorable for people who had this genetic mutation.

Tishkoff expects that the sophisticated machinery of genetics will also shed light on the holy grail of evolution questions – when and where modern humans arose. Based on multiple data, the time of origin is thought to be around 200,000 years ago, and it's generally accepted that Africa is the place, yet exactly where on the continent is still a mystery. “It is difficult to pinpoint ancestry,” Tishkoff said, “because populations move around.”

But impossible it's not. As Darwin did

in formulating his theory, Tishkoff has amassed a prodigious amount of data. Even more, she is drawing not only upon genetics but upon the expertise of other fields, such as paleontology and anthropology. Most fundamental of all, she has her predecessor's time-tested theory of evolution itself: All living organisms are descended from a common ancestor; descent with modification is the story common to all.

In a study recently published in *Science* (22 May 2009), Tishkoff and her international team released the largest-ever study of African genetic data, the culmination of more than 10 years of research. They traced the genetic structure of Africans to 14 ancestral population clusters and presented evidence that Africa has more genetic variation than anywhere else. The site of the most genetic diversity is in southern Africa along the border between Namibia and South Africa. That area is near the Kalahari Desert, the homeland of the Bushmen or San people, whose language is marked by characteristic click sounds. According to Tishkoff, “Our goal has been to do research that will benefit Africans, both by learning more about their population history and by setting the stage for future genetic studies, including studies of genetic and environmental risk factors for disease and drug response.”

– Martha Ledger

Heat-shock, or chaperone, proteins help other proteins to fold correctly – or cause them to be degraded if they're beyond repair. When operating properly, they preserve an organism's phenotype; when overstressed, they allow a host of variations to surface, which emerge as new traits in subsequent crossbreeding. Most of these traits are likely to be harmful to the organism, she explained, but occasionally something materializes that is valuable and that spurs the pace of evolution.

Haig H. Kazazian Jr., M.D., professor of genetics at Penn, spoke about retrotransposons as another kind of mechanism that generates variation. Retrotransposons are genetic elements that self-replicate and insert themselves into new sites. Four million years ago, there were 500,000 of them. Eighty to 100 retrotransposons are still active, six of which are highly active and account for one in every 600 to 800 mutations. As Kazazian put it, “It's an ongoing battle, with transposable elements trying to promote their own replication and the host developing defense mechanisms against them.”

Ancient in evolutionary terms and probably bacterial in origin, retrotransposons increase diversity and, said Kazazian, lead to new genes and new modes of regulation. They're the source of telomeres, the chromosomes' protective caps (whose internal presence on chromosome 2 was described earlier by Miller) and also the source of the proteins (RAG1 and RAG2) responsible for immunoglobulin diversity. Kazazian has successfully created a mouse model for human retrotransposition and is using it to study the range of traits controlled by various genes.

Retrotranspositions can also cause disease, especially when they insert themselves within, or even too close to, a gene. Kazazian has shown that some cases of hemophilia A are caused by an insertion on the X chromosome that in-

terferes with the synthesis of factor VIII, an element critical for clotting. Kazazian's lab is working on a variety of treatments that supply factor VIII to people who can't produce it, among them a gene therapy that uses a viral vector.

The goal of eliminating specific diseases – through an understanding of basic science mechanisms or the development of treatments, cures, and preventive measures – was shared by all the biomedical researchers. For example, Marjorie Oettinger, Ph.D., a professor of genetics at Harvard Medical School who discovered the RAG1 and RAG2 proteins mentioned by Kazazian, studies the immune system's recognition and response to antigens. Sarah Tishkoff, Ph.D., who is the David and Lyn Silfen University Associate Professor of Genetics and Biology at Penn, works with genetic variations that control susceptibility and resistance to diseases such as malaria and HIV infection. (See sidebar.)

If these biomedical researchers are successful, will their work, in turn, affect the trajectory of human evolution? Nobody touched on the long-term effects of medicine.

* * *

Except Miller, in his keynote address. In a characteristically humorous way, he noted that medicine is definitely a player in the evolutionary process. He related an anecdote about a medical school dean who asked incoming students for their definition of a doctor: "They gave some plausible answers ranging from 'well-trained technician' to 'deeply committed humanitarian,' but none was what the dean was looking for. 'A doctor,' he said, finally, when the students had run out of suggestions, 'is the person you go to so that natural selection doesn't work on you.'"

Medicine, he asserted, does have an effect. It allows the passage of traits that otherwise would be weeded out. And according to the "Surviving" exhibition,

humans, rather than being the perfect end-point of evolution, are, among other things, the repositories of several troublesome anatomical traits.

Human pelvises are narrow to facilitate an upright posture. Human craniums are large to accommodate larger brains. The combination makes childbirth painful and potentially lethal. The human jaw has its own drawback. Often it's too small for the 32 teeth housed there and its molars are often painfully impacted. An explanatory label in the exhibition suggests that people suffering the pain of impacted teeth would have trouble successfully finding mates and reproducing. In fact, 10 percent of today's population actually has fewer than four molars, which is a sign of natural selection working . . . oh, so slowly. Medicine – with its forceps, C-sections, and surgical extractions of impacted teeth – keeps narrow pelvises and small jaws in the gene pool.

As a result of these and other medical interventions, more people now populate the Earth than would have. Monge and Mann point out that, fewer than 500 years ago, only one in three children lived long enough to reproduce. Today, the vast majority of children grow up to have children of their own.

In a telephone interview, Monge acknowledged that medicine affects evolution. "It has already influenced the course of human life, extending it, and letting people live more healthfully." But she quickly added, "Most of the world lives in the medical past. Infant mortality in many places on this planet is as high today as it has been in the whole course of human history. And an even more deep and compelling statistic is the number of women who die in childbirth today in most of the developing world."

Still, in the developed world, biomedicine seems to be moving ahead at a breathless pace. In a film at the Museum's exhibition, the author, inventor, and futur-

ist Raymond Kurzweil predicts that, in the very near future, through a billion-fold increase in computing power, a technological evolution will occur that totally dwarfs the biological one. "By the late 2020s," he says, "nano-robots in our bloodstreams will be giving us direct intelligence," reporting on internal breakdowns and making internal repairs. To Kurzweil, it's natural for humans to move in this direction. In his pithy phrasing: "It's inherently human to go beyond our limitations."

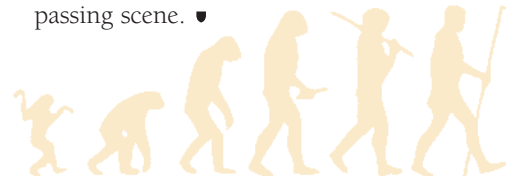
Kurzweil's vision raises all kinds of questions: To what extent will natural selection favor those with technology over those without it? Will the technologically sophisticated design themselves and replace natural selection as a shaping force?

Monge noted that more people have asked about Kurzweil's prediction than about any other part of the exhibition. But she wasn't surprised that the theory of evolution would stir up the deepest of issues.

"The idea of evolution," said Monge, "is so awesome, so part of everything about ourselves, our lives, our planet. It's something you have to spend some time with, at least on some level, to grasp the implications that it has on all our lives."

* * *

The colloquium ended late Friday afternoon, and it seemed that Darwin had been amply celebrated. It was already dark outside when I walked up to 33rd Street. The workday was over and people were streaming toward bus stops and parking lots. The evangelist was gone, and the sounds of traffic and footsteps filled the air instead. I had the sensation of having traveled through unimaginable time and into invisible spaces, and it took a few minutes to feel part of the passing scene. ▀



A PERSONALIZED VACCINE HELPS FIGHT RECURRENCE

VACCINES MADE FROM THE TUMOR CELLS OF PATIENTS WITH FOLLICULAR LYMPHOMA BOOST THE LENGTH OF DISEASE-FREE SURVIVAL.

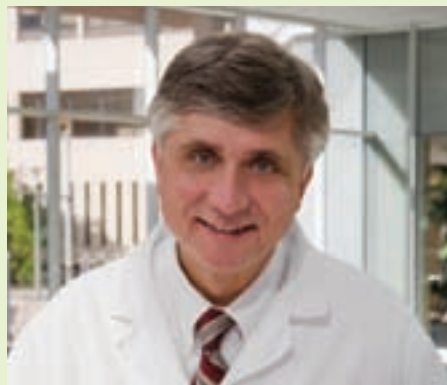
By Rabiya Tuma
and Holly Auer

Most patients with follicular lymphoma, a slow-growing form of lymphatic cancer that can transform into a more aggressive disease, initially respond to chemotherapy. But the disease frequently recurs and eventually it becomes resistant to available therapies. According to the Leukemia & Lymphoma Society, about 16,000 Americans develop follicular lymphoma each year, and those with the advanced disease usually die from it. At the annual meeting of the American Society of Clinical Oncology (ASCO) this spring, however, Stephen J. Schuster, M.D., associate professor of medicine in the division of Hematology/Oncology and a physician with the Abramson Cancer Center, presented findings that suggest promising new treatment strategies.

In a clinical trial conducted over eight years, Schuster's team treated patients with traditional chemotherapy, followed by a personalized vaccine made from the patients' own tumors. A second group of patients who had also responded to chemotherapy were given a control vaccine. Patients in the group that received the personalized vaccine had a median time of 44.2 disease-free months before relapse, compared to 30.6 months for patients in the second group. That amounts to an increase of 44 percent.

"Whether the vaccine eradicated the disease that could no longer be seen on CT scan for patients in remission or just controlled minimal residual disease remains to be determined," says Schuster. Still, as he puts it, "Even slowing the recurrence rate would be an amazing achievement because, in this study, we used this vaccine to improve patient outcomes after a single series of immunizations, and many vaccines require booster shots, which were not part of the original trial."

The personalized vaccine used in the Penn study included tumor-derived idiotype protein – a protein unique to each lymphoma tumor – that is isolated from individual patient samples and attached to the hemocyanin protein from a kind of sea snail called the keyhole limpet. Because it is safe in humans, keyhole limpet hemocyanin is highly prized as a carrier of vaccines. The protein is injected into the patient simultaneously with an



Stephen J. Schuster, M.D.

agent called GM-CSF that stimulates the immune system. The control vaccine included the keyhole limpet hemocyanin protein plus GM-CSF.

Although idiotype vaccines have been tested in the past, this is the first trial to show a statistically significant improvement in progression-free survival in follicular lymphoma patients treated with an idiotype vaccine. According to the *NCI Cancer Bulletin* (6/2/09), it was one of the results that "generated intense interest" at the ASCO meeting. Previous trials included patients who had partial or complete responses; in this trial, on the other hand, the investigators vaccinated only patients who had no detectable tumor remaining after chemotherapy. Under these

conditions, the investigators hypothesized that the vaccine could hold minimal residual disease in check.

When the trial started, chemotherapy was the standard of care for previously untreated patients. Since that time, the standard of care has evolved to include chemotherapy plus the antibody rituximab (Rituxan®). The next step, in Schuster's view, is to launch a clinical trial to test whether adding a personalized vaccine to the current standard of chemotherapy and rituximab will improve patient outcomes. "If indeed our trial is right that this approach leads to improvements in progression-free survival, then adding it to even more effective therapies like chemotherapy plus Rituxan® might result in even greater benefit."

Although both rituximab and the tumor vaccine tested in this trial are immunologic agents, they work by different mechanisms. Rituximab is a mass-produced antibody designed to attack the type of cell that has gone awry in follicular lymphoma. By contrast, the newly tested personalized vaccine induces the patients' own immune systems to attack their tumors based on a protein that is expressed uniquely by their own tumor cells.

In addition to the immediate clinical results, the trial will provide an important opportunity for biomarker discovery in the future. Tumor samples were collected from all of the patients who enrolled in the trial. "This is a treasure trove of material," Schuster says. "It is a rare opportunity to have outcomes data with the corresponding banked viable tumor cells and tumor infiltrating cells present for analysis. This is an opportunity for learning that cannot be passed up." ■

What's New in Alzheimer's Research?



For the Penn Medicine faculty members who investigate Alzheimer's disease, 2009 so far has been a year of advances, some major funding, and recognition beyond the usual academic and research spheres. That recognition comes in part from two independently produced documentaries – *Alzheimer's Disease: Facing the Facts*, a one-hour documentary that aired on PBS affiliates earlier this year, and *The Alzheimer's Project*, a four-part series produced for HBO that aired in May.

Facing the Facts begins with a sequence of people talking about their plans for their “golden years.” They could be our neighbors. They could, in fact, be ourselves. Next, the camera pans over a montage of newspapers and magazines, all featuring headlines about promising new directions in the fight against Alzheimer's disease. All of them are optimistic – and, up to this point, all unrealized. The narrator, in the calm voice of actor Edward Herrmann, informs us that more than five million Americans suffer from Alzheimer's disease. “No one is spared,” he says, right after a film clip shows President Reagan speaking at a lectern. Then Penn's John Q. Trojanowski, M.D., Ph.D., is shown, telling us that the incidence of Alzheimer's disease “goes up exponentially after age 65.” The narrator calls AD “irreversible brain failure.”

If facing the facts about AD also means hoping fervently for a cure or a palliative treatment while feeling the anguish of the afflicted persons and their families, the

producers have done their job well. One patient had run away six times at the time of filming; he also seems unable to control the urge to whistle tunelessly. “He doesn't know his name,” his wife tells us, adding that AD “is a crushing blow” for someone who had been a brilliant man.

Trojanowski, professor of pathology and laboratory medicine, director of the Institute on Aging, and director of the Alzheimer's Disease Center, is not the only Penn researcher in the documentary. Virginia Lee, M.D., M.B.A., director of the Center for Neurodegenerative Disease Research, is glimpsed consulting with Trojanowski, her husband. Mark Forman, M.D., Ph.D., assistant professor of pathology and laboratory medicine and co-director of the Neurodegenerative Disease Brain Bank, is shown explaining how the brains of Alzheimer's patients are smaller than healthy brains; the shrinkage results from the widespread death of neurons. Now at Merck Research Laboratories, Forman has an adjunct appointment at Penn. Christopher Clark, M.D., an associate professor of neurology and former director of the Penn Memory Center, notes that AD “starts in mid life, silently eating away at the brain.” He would like to see biomarkers for the disease incorporated into routine screening, to detect it earlier on when there may still be a chance to treat it.

Several other prominent experts from across the nation appear in the documentary, including John C. Morris, M.D., of Washington University in St. Louis, who

fears that AD will “reverberate” through our society and even threaten to bankrupt the nation's health-care system. But it is Trojanowski who bluntly confronts the issue of funding. He cites with approval the “public-private pact” that raised funds to combat polio. So far, he asserts, Alzheimer's researchers are underfunded – they need to go after a *hundred* targets, not only a few.

The Alzheimer's Project, presented by HBO and the National Institute on Aging, has a different focus for each of the four parts. The grim statistics about AD are shown on the screen. “54% of Americans Are Touched By It” – meaning the family repercussions. Even grimmer: “10 Million Baby Boomers Will Develop It.” On the other hand, as we hear Virginia Lee put it near the beginning of “Momentum in Science,” there's been a “miraculous” increase in knowledge over the last 25 years. The episode touches on several aspects of research across the United States, such as the quest to find out why the beta-amyloid plaque is killing neurons and how brains are retrieved for scientific research, sliced, frozen, and stored. Gerard Schellenberg, Ph.D., now a professor of pathology and laboratory medicine at Penn, is featured in the “chapter” on genetics. Although he notes that the causes of early-onset AD are quite clear, the causes of the late-onset form are much more difficult to understand. Still, he expresses confidence that investigators will be able to identify a

group of “susceptibility factors” and find good targets for drugs. One reason for his optimism: “The technology that we’re using is just phenomenal.”

The research of Lee, Trojanowski, and Schellenberg is also discussed in *The Alzheimer’s Project: Momentum in Science*, a companion book to the series, published by PublicAffairs.

In March, a team of Penn researchers led by Leslie M. Shaw, Ph.D., professor of pathology and laboratory medicine, announced that it had validated and standardized a test that could confirm or rule out Alzheimer’s disease in patients. The study was published in the on-line edition of the *Annals of Neurology*. By measuring concentrations of cerebrospinal fluid (CSF) of two of the disease’s biochemical hallmarks – amyloid beta42 peptide and tau protein – the test also predicted whether a person’s mild cognitive impairment would develop into Alzheimer’s disease over time. Because the investigators were able to detect the devastating disease at the earliest stages, before the symptoms of dementia appeared and irreversible damage occurred, the findings hold promise in the search for effective pharmaceutical therapies capable of halting the disease.

The new test builds on previous research that identified a pathological CSF biomarker signature. The Penn Medicine team found evidence of neuron degeneration – marked by an *increase* in CSF concentration of tau proteins – and plaque deposits, indicated by a *decrease* in the concentration of amyloid beta42. They also found that people with two copies of the genetic risk factor for Alzheimer’s disease, APOE e4, had the lowest concentrations of amyloid beta42, compared to those with one or no copies.

“Validated biomarker tests will improve the focus of Alzheimer’s clinical trials, enrolling patients at earlier stages of the disease to find treatments that can at

least delay – and perhaps stop – neurodegeneration,” said Shaw, co-director of the Penn Alzheimer’s Disease Neuroimaging Initiative Biomarker Core. “In addition, prevention trials can test methods to delay or block mild cognitive impairment from converting to full-blown Alzheimer’s.” Further studies to validate the test are under way.

According to the researchers, the test was 87 percent accurate overall (80 per-

A team of Penn researchers has validated and standardized a test that could confirm or rule out Alzheimer’s disease in patients. It also predicted whether a person’s mild cognitive impairment would develop into Alzheimer’s disease over time.

cent or above is considered clinically useful). It accurately ruled out Alzheimer’s disease in 95.2 percent of the subjects and accurately predicted the conversion from mild cognitive impairment to Alzheimer’s disease at a rate of 81.8 percent. And, as Trojanowski notes, the test involves “a safe, simple lumbar puncture.”

Schellenberg made news again in April, when it was announced that he had received a five-year grant of \$18.3 million from the National Institute on Aging to lead a multi-institutional genome-wide association study. Its goal is to identify genes that may affect the risk of developing Alzheimer’s disease. Ge-

nome-wide association studies require a large number of samples to be studied in order to detect significant change. Existing phenotype data and DNA samples gathered by Alzheimer’s Disease Centers across the nation will be analyzed by the Alzheimer’s Disease Genetics Consortium, which was formed to collect additional samples.

Researchers will look for susceptibility genes that may influence when a person gets the disease and how fast it progresses. They also hope to identify genes that influence specific biomarkers related to AD, such as the amount of amyloid plaques or neurofibrillary tangles, concentrations of amyloid beta and tau in cerebral spinal fluid, the rate-of-disease progression, and responses to environmental factors such as drugs.

Schellenberg came to Penn last year, after what the newsletter of Penn’s Institute on Aging describes as “a decade of courting.” He had been at the University of Washington and the Veterans Affairs Medical Center in Seattle, but had collaborated for several years with Trojanowski and Lee. As he put it, “I came to realize that at Penn, there is a combination of superb faculty, strong support from the School of Medicine, and a strong emphasis on collaboration, making this a great place to do research.” Schellenberg is credited with discovering the Presenilin 2 gene, which is linked to early- and late-onset Alzheimer’s disease.

In June, *Alzheimer’s Disease: Facing the Facts* won an Emmy in the documentary category from the Boston/New England Chapter of the National Academy of Television Arts & Sciences. The executive producer and writer of *Facing the Facts* is Carol Edwards, associate director of the Penn Memory Center’s Education and Information Transfer Core. With Glenn Orkin, co-owner of Motion, Inc., in Hartford, Conn., she wrote, edited, and produced the film. ♥

Gregory Ginsberg, Master



When Gregory G. Ginsberg was a youngster, his father would take home movies of birthday parties, picnics, and family trips. His father, a gastroenterologist, used that same camera to film some of his more interesting cases. Unfortunately, he never got the hang of switching the film.

“So we’d be watching a movie of a party and it’d be going along, and all of a sudden there’d be a bleeding ulcer or colon cancer,” says Ginsberg. “It wasn’t subliminal.”

Unlike some doctors, Ginsberg had a sense of his career path at an early age. “I pretty much knew by the sixth grade that I wanted to go into gastroenterology,” he says. “I think it offers the ideal blend of cognitive and procedural challenges.”

Now professor of medicine and director of endoscopy for the University of Pennsylvania Health System, Ginsberg was the 2005 recipient of the School of Medicine’s Luigi Mastroianni Jr. Clinical Innovator Award. More recently, he was named the Distinguished Educator of the

American Society for Gastrointestinal Endoscopy (A.S.G.E.) and will take over as president of the society in 2010.

One of the Awards of Excellence given each year to high-achieving faculty members, the Mastroianni award acknowledges clinical innovation and technologically based research. Anil K. Rustgi, M.D., chief of the Division of Gastroenterology, nominated Ginsberg for the award.

“At a national level, he’s recognized as an elite authority on interventional endoscopy from the point of procedures to deal with pre-neoplastic and early neoplastic diseases of the stomach, intestines, and colon,” says Rustgi. “He’s very innovative in developing new technologies for the diagnosis of G.I. diseases and tries to marry research in the animal settings with human-based trials to advance patient care.”

Ginsberg is asked to speak around the world, and many of his talks are focused on “the holy grail” of gastroenterology – us-

ing enhanced endoscopic mucosal imaging to catch and remove abnormalities before they develop into problems like those associated with Barrett’s Esophagus. The procedure involves using stains or contrast to be able to detect changes happening in the mucosa along the esophagus and the stomach, which could be signs of early cancer. Increasingly, doctors are using electronic means to enhance these changes, and Ginsberg is exploring super-high magnification techniques that allow imaging at the cellular level in living tissue through the endoscope.

As Ginsberg puts it, “The hope is that early detection will help prevent the development of advanced disease.”

Ginsberg is also known for his work in transendoscopic surgery, a new field of medicine in which surgeons operate through natural openings in the body instead of slicing through muscles and organs. The new approach can lessen healing time and prevent complications.

of Endoscopy

By Dawn Fallik

Photographs by Addison Geary.

David Fleischer, M.D., was Ginsberg's mentor while he was a fellow at Georgetown University Medical Center and is now professor of medicine at the Mayo Clinic College of Medicine in Arizona. Fleischer flat-out asserts that Ginsberg is no good at judging the performance of Philadelphia sports teams (the two have an ongoing bet). On the other hand, he is just as eager to say that Ginsberg excels at creative approaches to diagnosis and surgery.

In particular, Fleischer points to Ginsberg's use of magnets – one in the stomach and one in the small intestine – to create a natural hole instead of doing surgery to remove part of the digestive tract. The two magnets would close by magnetic force, eliminating the need for surgery.

"He doesn't necessarily think about what's possible based on what's been done," says Fleischer. "He looks at what he has and thinks of new approaches. That's what makes him such a good endoscopist – he's not just good technically, he's got a creative mind."

The magnets have been used experimentally in two ways. One is to place them inside two different pathways, so that the magnets – which naturally try to cling together – create a hole without having to perform surgery. For example, used between the stomach and the small intestine, they essentially create a gastric bypass route.

Magnets have also been used to transiently anchor the bowel to the anterior abdominal wall, creating a minimally invasive way to feed directly into the small intestine.

"This approach is life-saving in countless patients with disordered oral intake of nutrition," explains Ginsberg. "We are working on bringing these approaches to clinical use."

Ginsberg is married with four daughters. His wife, Jane Ginsberg, describes him as a man with a real zest for life – for his work, his students, and his family.

"There have been countless days when his face reveals the stresses of having to diagnose and reveal a cancer or inoperable tumor to a patient. I know it is still very emotional for him and that he treats each patient and their family with dignity and respect."

Ginsberg's former mentor says that combination of professionalism and



Assisted by Cyril English, an endoscopy technician, Gregory Ginsberg prepares to begin a procedure.

compassion helps make Ginsberg "a triple threat."

"Success in medicine is measured in three ways," Fleischer continues. "As a teacher, can you do good research? As a doctor, can you take good care of your patients? And as a person, can you have a family life? He manages all three."

Both Ginsbergs grew up in the Philadelphia area and were happy to come to Penn. The school was a "perfect fit," they

say, because the clinical practice provides a wide range of challenges as well as the opportunity to teach.

"What keeps me at Penn are the patients and the people," says Ginsberg. The opportunity to have a beneficial impact on patients with challenging medical problems "remains an immense source of professional satisfaction."

In particular, Ginsberg says, he is proud of the Endoscopy Center at the recently opened Perelman Center for Advanced Medicine, and he believes the Advanced Endoscopy Fellowship training program is among the most competitive in the nation. While the layout and staffing in the new endoscopy center provide a better experience for patients, it was also cited in this year's inaugural A.S.G.E. Endoscopy Unit Recognition Program for promoting excellence in the specialty.

"The state-of-the-art instrumentation provides high-definition imaging and all manners of diagnostic and therapeutic endoscopy, including advanced polypectomy, endoscopic ultrasound, ERCP, and more," says Ginsberg.

In the end, however, it's the challenge of gastroenterology more than the instruments that keeps him intrigued. A patient will come in with a set of symptoms and it's like a puzzle – and not just a physical puzzle. Often, the physician must also consider emotional issues like anxiety, and it's up to him to figure out how to alleviate the symptoms and to get to the root of the problem.

Now that he has 20 years of practice behind him, Ginsberg says he's learned to be more patient – both with others and himself.

And while none of his daughters is on the gastroenterology path, he still keeps his father's home movies around, just in case. ♥



Development Matters

DONOR'S CHOICE: MANY WAYS TO MAKE

“The noblest question in the world is, what good may I do in it?” – Benjamin Franklin

Penn Medicine donors are capable of remarkable things: from the re-shaping of our medical campus along the banks of the Schuylkill, to supporting vital educational and patient programs. Each day, our supporters help us transform lives.

The measure of our donors' impact, however, is reflected not only in the number of dollars raised, but also by the creativity shown in their distinctive philanthropy. For so many individuals, supporting Penn Medicine is a deeply personal choice, and their generosity illustrates that fact.

People from all walks of life give back to express profound appreciation for the gift of life. They joyfully celebrate healthy milestones as well as the treasured memories of loved ones. They act on their steadfast belief that medicine – and the arduous training of its practitioners – can change countless lives in Philadelphia and beyond.

In this installment of “Development Matters,” we introduce you to some of Penn Medicine’s dedicated friends and supporters. Each has found a unique way to honor his or her relationship with our institution while creating a lasting benefit for our students, faculty, and patients.

Devotion to Elderly Patients Prompts Geriatric Award

Every night after dinner, Sarle H. Cohen, M.D. '55, would spend hours on the phone talking with his patients and their families. Throughout his nearly 50-year career in internal medicine, Dr. Cohen made it a practice to spend this time explaining treatment options and plans, offering comfort and advice during difficult moments. “There weren’t many doctors like him,” says his widow, Barbara. “He was an incredibly devoted physician – patient and kind.”

When Dr. Cohen passed away in May 2008, his family looked for an opportunity to memorialize and continue his legacy of compassionate patient care. Working with Penn Medicine, the Cohen family created the **Sarle H. Cohen, M.D., Endowed Fund**. This fund will support a financial award to a medical student who shows a commitment to providing older patients with outstanding care, through leading-edge research as well as kindness and caring attention. The family made a pledge of \$50,000 to be paid over five years.

“We hope that the Sarle H. Cohen, M.D., award will increase visibility of geriatric medicine as well as health-care issues surrounding the elderly,” said Barbara. “We clearly need

people of talent and quality in the field, and we would like to honor a student that chooses to pursue this direction in medicine. This award really sums up what Sarle did so well.”

To learn more about supporting your medical alma mater with an endowed fund, contact Vanessa Marinari at 215-898-5164 or marinari@upenn.edu.

Born Forty Years Ago, A Classroom for the Future

Forty years ago, three medical students – Louis Kozloff, C '65, M.D. '69, Edward Anderson, C '65, M.D. '69, and William Moreau Thompson, M.D. '69 – became close friends and banded together to tackle the rigors of medical school. Now, to celebrate their 40th reunion and their enduring friendship – and inspired by the memory of their long study sessions – the class-



Classmates, friends, and now donors: from the left, Louis Kozloff, Edward Anderson, and William Moreau Thompson visit the house they shared as med students. The three are supporting a classroom in the School of Medicine’s new education space.

AN IMPACT AT PENN MEDICINE

mates have joined to provide today's medical students with an ideal place to learn.

The Anderson Kozloff Thompson Classroom in the School of Medicine's new education space is a key component of the School's renovation plans. It will feature state-of-the-art multimedia and information technology. The room can also be reconfigured for small group learning or expanded to accommodate larger groups for lectures.

Dr. William Thompson is proud of their gift and hopes that it will inspire others to give. "I really consider it an honor to be part of the Anderson Kozloff Thompson Classroom, and I hope the three of us will serve as a model for alumni to honor their alma mater," he says.

In addition to paying homage to the School of Medicine, the classmates wanted to leave a lasting legacy and have their names aligned with excellence in medical education.

"We all love the fact that we will be able to take our grandchildren to campus and show them a state-of-the-art space with our names on it. The renovations for the School of Medicine are exciting, and we are thrilled to contribute," says Dr. Louis Kozloff.

"I hope we will serve as a model for alumni to honor their alma mater."

"Each of us contributed a nice-sized gift and, all put together, it made a huge impact."

Dr. Edward Anderson, a former trustee of the University of Pennsylvania, says, "I look back fondly on our education and how prepared we were for our respective fields. My hope is the students will utilize the classroom to further enhance their knowledge and make lasting friendships as well."

For more information about the new School of Medicine education space, contact Vanessa Marinari at 215-898-5164 or marinari@upenn.edu.

Cancer Survivor Sponsors Patient Education Conferences

Dealing with a cancer diagnosis and treatment is a difficult journey for both patients and their families. To assist patients through every phase from diagnosis through long-term survivorship, the Abramson Cancer Center each year hosts informative, interactive, **daylong patient education** conferences on many specific types of cancer.



Chief of Hematology/Oncology Lynn Schuchter, M.D., (right) chats with some patient conference attendees. The conference was sponsored by George Graham, a cancer survivor, and his wife, Elizabeth.

The ACC Conferences – the only conferences of their kind in the region – have provided a powerful way for one particular cancer survivor to give back and help fellow patients cope with the disease. Recently, George Graham and his wife, Elizabeth, made a generous gift in support of the ACC "Focus on Melanoma Patient Education Conference."

George explains his motivation to support programs like these, saying, "As a melanoma survivor, I remember the feelings of shock and despair after being diagnosed and the subsequent struggles to understand the available treatment options. I was lucky to find a few wonderful melanoma patients who took the time to help me learn from their experiences and tackle the battle I would fight against this terrible cancer."

"I hope these sessions will help both patients and their families better understand their treatment options and find the strength to defeat this disease."

For information about how you can sponsor a patient education conference, contact Tricia Bruning at 215-898-1033 or tbruning@upenn.edu.

Bioethics Legend Inspires Lectureship

In one of the most eagerly anticipated lectures of the year, the dynamic Paul Farmer, M.D., Ph.D., visited the Penn campus to speak at the inaugural **Renée C. Fox Lectureship in Medicine, Culture, and Society**. More than 500 students and faculty members attended the event, designed to embody the interdisciplinary spirit of Penn Professor Renée Fox's legendary career as well as to reflect the prestige and tradition that is Penn.



Dr. Renée C. Fox greets Dr. Paul Farmer, the inaugural speaker for the Fox Lectureship.

Dr. Farmer, the Presley Professor of Medical Anthropology at Harvard Medical School, is a founding director of Partners in Health. He and his colleagues have pioneered novel, community-based treatment strategies for treating AIDS and tuberculosis; his “grand rounds” lecture focused on global health equity.

The lectureship was established by Dr. Fox’s sister and brother-in-law, Rosa and Robert Gellert, on the occasion of her 80th birthday. The Gellerts made a single gift of \$25,000 to create the lectureship that commemorates Dr. Fox’s work. Numerous friends, colleagues, former students, and faculty members made additional contributions in order to ensure that the series continues long into the future.

“We wanted to take this opportunity to honor Renée while she was still actively pursuing her work,” explains Robert Gellert. “We wanted to make sure her name will continue to live at Penn.”

“Dr. Renée Fox is, without question, one of the most respected figures in medicine, sociology, and ethics,” says Arthur H. Rubenstein, M.B.,B.Ch., executive vice president of the University of Pennsylvania for the Health System and dean of the School of Medicine. “Lectureships are a vital vehicle for exchanging ideas, and this particular lectureship is a wonderful tribute to a remarkable and influential scholar.”

For more information about supporting clinical programs at Penn Medicine, contact Kim Grube at 215-746-3007 or kimgrube@upenn.edu.

Making History: One Gift at a Time

The ultimate goal of Penn Medicine’s \$1 billion “Making History” campaign is to focus our efforts on the most pressing medical challenges of our time. Gifts to Penn Medicine, including those to our annual funds, allow our health-care professionals to advance healing and attract and retain the best minds that drive medical education, research, and patient care. With payment plans that allow you to fulfill your pledge of \$25,000 or more over five years, your contribution can make a tremendous impact at Penn Medicine. Each gift, no matter the amount, has the power to touch millions of lives and create a healthier world for us all.

We are very pleased to report that, as of press time, the total dollars raised in fiscal year 2009 was approximately **\$145 million**. Our second highest total to date, this is a positive and strong result for a difficult year. We thank you for your many generous contributions and look forward to earning your continued support during the challenging fiscal year ahead.



Recent Gifts

The **Bill & Melinda Gates Foundation** recently awarded Penn Medicine’s Gene Therapy Program a three-year, \$3.2 million grant to research the impact of adenovirus infections, such as pneumonia and gastroenteritis, on HIV-1 vaccine performance.

James J. and Frances M. Maguire have increased their commitment to \$3 million to support the translational cancer research of Stephen J. Schuster, M.D., whose innovative work aims to improve the diagnosis and treatment of lymphoma through epigenetics, imaging, signal transduction, and immunotherapy.

The **Donald W. Reynolds Foundation** awarded The Penn CARES (Community and Academic Resources for Education about Seniors) Program a \$1.9 million grant to establish a comprehensive longitudinal curriculum for medical students, augment teaching on an Acute Care for Elders (ACE) unit, and substantially increase the expertise in geriatric medicine among key faculty teachers and chief residents.

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

Alumni Events

You can find out more about these and other upcoming events at www.med.upenn.edu/alumni/calendar. Please email any questions to PennMedicine@alumni.med.upenn.edu.

September

- Tuesday, September 29 – Council of Young Alumni Meeting, Philadelphia
- Tuesday, September 29 – Back to School Night with the Phillies, 5:30 – 10:30 p.m., Philadelphia
- Wednesday, September 30 – Medical Alumni Advisory Council Meeting, Philadelphia

October

- Tuesday, October 6 – Otolaryngology Reception, 6:00 – 8:00 p.m., San Diego
- Tuesday, October 13 – Surgery Reception, 6:00 – 8:00 p.m., Chicago
- Thursday, October 22 – Mitchell J. Blutt, M.D., Visiting Professorship in Entrepreneurship Lecture, 2:00-5:00 p.m., Philadelphia
- Sunday, October 25 – Ophthalmology Reception, 7:00 – 11:00 p.m., San Francisco



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Senior Director, Alumni Development and Alumni Relations
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'40s

C. Everett Koop, M.D., G.M.E. '47, Sc.D., former U.S. Surgeon General, was among those who received a 2009 Raymond and Beverly Sackler Award for Sustained National Leadership from Research!America. The award, presented in March, recognizes Koop's decades-long commitment to advocacy for public health. Currently the Elizabeth DeCamp McNerny Professor of Surgery at Dartmouth Medical School, Koop served two terms as Surgeon General (1981-1989), becoming the government's chief spokesperson on AIDS at the outset of the AIDS crisis. He is widely credited with tackling some of the nation's most daunting public health challenges, most notably tobacco addiction and HIV/AIDS. A steadfast advocate for public health education, he has written extensively on public health issues. His many honors and awards include 41 honorary doctorates and the 1995 Presidential Medal of Freedom.

'50s

Harold J. Robinson, M.D. '57, Narberth, Pa., a retired cardiologist, reports that he won the Commerce Bank Award for an original painting entered in a juried exhibition at the Wayne Art Center.

'60s

David F. Apple Jr., M.D. '62, was named emeritus medical director of the Shepherd Center in Atlanta, which is devoted to the medical care and rehabilitation of people with spinal cord injury and disease, acquired brain injury, multiple sclerosis, and other neuromuscular problems. He served as

the director from 1975 to 2005. For his years of service, Apple was inducted into the National Spinal Cord Injury Association Hall of Fame in 2008.

Richard M. Schieken, M.D. '65, G.M.E. '69, reports that he retired as chairman of the Division of Pediatric Cardiology at Virginia Commonwealth University-Medical College of Virginia in 2002. He was a professor of pediatrics and of human genetics there and continues to teach part time at Virginia Commonwealth's medical school in the Foundations of Clinical Medicine course. In 1998, he received an M.S.H.A. degree from Virginia Commonwealth's School of Health Administration. At Virginia Commonwealth and earlier at the University of Iowa, he held a Preventive Cardiology Academic Award from the National Heart, Lung, and Blood Institute. He also served on the executive committee and the advisory committee of the institute's National Cholesterol Education Program.

'70s

Robert I. Rudolph, M.D. '71, G.M.E. '75, was named the Duhring Clinic Attending of the Year for excellence in teaching by Penn's Department of Dermatology this spring. A clinical professor of dermatology at Penn, he has been a member of the department's faculty since 1975.

Rita F. Redberg, M.D. '82, M.Sc., professor of medicine at the University of California at San Francisco and director of cardiovascular women's services for the U.C.S.F. National Center of Excellence in Women's Health, was honored in May for her work in advancing women's heart health at the 5th Annual Bay Area Go Red for Women Luncheon. Go Red for Women, created by the American Heart Association, helps fund cutting-edge research, conducts public and professional educational programs, and advocates for the protection of women's heart health. Redberg was recognized for her important role in advancing the initiative. Cofounder of

the U.C.S.F. National Center of Excellence in Women's Health, she also chairs the Choose to Move Science Advisory Group for the A.H.A. She has served on many other A.H.A. committees and chairs the American College of Cardiology/ American Heart Association Primary Prevention Performance Measures Writing Group. In 2003, she took a one-year sabbatical from U.C.S.F. to serve as a Robert Wood Johnson Health Policy Fellow in the office of Sen. Orrin Hatch in Washington, D.C.

'80s

Richard E. Besser, M.D. '86, was acting director of the Centers for Disease Control and Prevention in Atlanta. He took his residency in pediatrics at Johns Hopkins University Hospital and has worked in the C.D.C.'s Epidemic Intelligence Service. In the early 1990s, he tracked down the source of an *E. coli* outbreak in the Boston area. After serving as director of a pediatric residency program in San Diego for two years, he returned to the C.D.C. in its Respiratory Diseases Branch, where he started "Get Smart: Know When Antibiotics Work," its national campaign to promote appropriate use of antibiotics.

Kristine Yaffe, M.D. '89, G.M.E. '90, a professor in the departments of Psychiatry, Neurology, and Epidemiology at the University of California at San Francisco, received a three-year, \$240,000 grant from the Alzheimer's Association to lead a study about the predictors of mild cognitive impairment (MCI) or dementia among women 85 and older. The researchers will determine how many of the participants in the study have MCI or dementia and measure which of these participants have specific potential risk factors, such as lack of social support, lack of physical activity, smoking, diabetes, cardiovascular disease, depression, and other factors. Yaffe serves as associate chair of research for the Department of Psychiatry at U.C.S.F.

'90s

Paul P. Weitzel, M.D. '95, an orthopaedic surgeon and assistant clinical professor at Tufts University School of Medicine, was named vice president of medical affairs for Orthopaedics by Serica Technologies. Serica is a medical-device company that pioneers silk-based biomaterials for tissue regeneration. Weitzel specializes in sports medicine with an emphasis on minimally invasive arthroscopy of shoulders and knees. He is affiliated with the New England Baptist Hospital and practices at the Boston Sports and Shoulder Center.

OBITUARIES

Charles M. Howell Jr., M.D. '37, Winston Salem, N.C.; November 8, 2008. He joined the United States Air Force as a flight surgeon and earned the rank of major before he was honorably discharged. He was chairman of the Department of Dermatology at the Bowman Gray School of Medicine at Wake Forest University for 27 years. At an age when most doctors have retired, he opened a private practice in 1983 and continued to practice into his 90s.

Carl K. Friedland, M.D. '39, G.M.E. '43, Winston Salem, N.C.; March 6, 2009. He practiced internal medicine in Dover, N.J., for 23 years and started the panel of electro-cardiographers at Dover General Hospital, where he was chairman of the division of pulmonary medicine. He taught the parallel curriculum at the Bowman Gray School of Medicine of Wake Forest University and had also been an assistant professor of medicine at the New Jersey College of Medicine and Dentistry. In 1952, he was elected a fellow of the American Board of Physicians.

George F. Stoll, M.D. '39, Ocean Grove, N.J., a retired physician who had maintained a practice in Belleville; January 31, 2008. In 2007, he received a Special Recognition Award from the Historical Society of Ocean Grove.

Stephen T. Whelan, M.D. '40, Gladwyne, Pa., a retired dermatologist; May 8, 2009. During World War II, he was an officer with the Public Health Service in the Canal Zone. He had been a staff physician at Mercy Fitzgerald Hospital in Darby and later served at Delaware County Memorial Hospital, where he had been chief of dermatology. He had also been an adjunct professor at Penn's School of Medicine. In 1976, Bobbs-Merrill published *Making Sense Out of Sex: A New Look at Being a Man*, which Whelan wrote with his daughter-in-law, Elizabeth Whelan, president of the American Council on Science and Health.

Jack E. Cole, M.D. '41, Bethlehem, Pa.; January 29, 2008. In World War II, he was in the U.S. Army, where he received a Purple Heart and a Combat Medic badge. After taking his internship at Wilkes-Barre General Hospital, he went on to practice family medicine in Matamoras, Pa., until 1947 and served as a staff member for St. Luke's Hospital in Bethlehem. He also practiced family medicine in Bethlehem 1952-68 and 1973-89. Cole was an incorporator and member of the medical staff at Muhlenberg Hospital and a student-health physician at Lehigh University 1948-52. From 1968 to 1973, he was a physician in the Peace Corp in Afghanistan, Swaziland, and India. He was a preceptor at Temple University Medical School 1978-86 and received the school's Recognition Award. He was a diplomat of the American Board of Family Practice and a fellow of the American Academy of Family Physicians. His books include *Wandering Voices: A Collection of Verse*, published in 1999.

Robert E. Booth Sr., M.D. '43, G.M.E. '45, Gladwyne, Pa., a retired radiologist; March 10, 2009. For two years, he served as the only radiologist at the U.S. Naval Hospital and at Municipal Hospital in Key West, Fla. In 1948, he became the first chairman of the Department of Radiology at Underwood Memorial Hospital in Woodbury, N.J., a position he held for 36 years until 1985. Simultaneously he was chairman

of the Department of Radiology at the Elmer Community Hospital. He developed three large private-practice radiology offices in Southern New Jersey. He had been president of the medical staff at Underwood Memorial Hospital, president of the Medical Staff at Elmer Community Hospital, and president of the Medical Club of Philadelphia. A member of the American College of Radiology, he served on the executive board of the Philadelphia Roentgen Ray Society.

Robert B. Chodos, M.D. '43, Saratoga Springs, N.Y., retired head of nuclear medicine at Albany Medical Center; September 29, 2008. He served in the U.S. Navy during World War II. Former head of nuclear medicine at the U.S. Veterans Hospital in Albany, he was also an adjunct professor of physics at the University of Albany. He was a fellow of the American College of Physicians, of the American Federation of Clinical Research, and of the New York Academy of Sciences. He had served as associate editor of the *Journal of Nuclear Medicine*. As a medical student, he was elected to Alpha Omega Alpha.

Harry B. O'Rear, M.D. '43, Waynesville, N.C., retired vice chancellor of health affairs for the University of Georgia; October 30, 2008. A pediatrician, he served for 12 years as president of the Medical College of Georgia. Before that, he had been a member of the faculty at Duke University. During World War II, he was a U.S. Army medical officer in the Philippines.

Anne Wight Phillips, M.D. '43, G.M.E. '47, Weston, Mass., described by newspaper reports as the first woman surgeon to operate at Massachusetts General Hospital; February 12, 2009. Her first residency was at Burlington County Hospital at Mount Holly, N.J. She had wanted a senior surgical residency, but because Burlington County had none open to women, she moved on to Laird Memorial Hospital in Montgomery, W.Va. In the late 1940s, Phillips trained briefly at the Oak Ridge Institute of Nuclear Studies in Tennessee. While there, she served on the federal Atomic

Energy Commission. Phillips became nationally recognized in the field of burn research and fire prevention and, in 1973, President Nixon appointed her to the National Commission on Fire Prevention and Control. In 1974, Phillips founded the nonprofit Smoke, Fire and Burn Foundation and served as its director for 30 years. There she developed the first school "smoke drill," which, her son said, "was taught to millions of schoolchildren across the country." She took part in creating fire safety films and stronger standards for flammable fabrics and talked about fire safety at local schools. Three years ago, the Home Safety Council and the Congressional Fire Services Institute, representing the fire caucus on Capitol Hill, established the Anne W. Phillips Award to recognize the contributions of others in the same cause. At 87, Phillips published a novel, *The Corners In Time*, about a woman who becomes a doctor and the struggles she faced. Her second novel, *The Foothills of Happiness*, is scheduled for publication.

Truman G. Schnabel Jr., M.D. '43, G.M.E. '47, Bryn Mawr, Pa., the C. Mahlon Kline Emeritus Professor of Medicine and the Distinguished Emeritus Professor of Medicine; March 10, 2009. He served as an Army captain in a medical battalion in the Philippines in WWII. After his discharge, he completed his residency in internal medicine at Massachusetts General Hospital, then returned to the University of Pennsylvania as a cardiology fellow. In the late 1940s, he helped establish the first cardiac catheterization unit at the Hospital of the University of Pennsylvania. In 1954, he was appointed an assistant professor of medicine at Penn, following in the footsteps of his father (M.D. 1911). Two years later, he was promoted to associate professor. In addition to teaching, he was assigned to Philadelphia General Hospital, the first full-time Penn professor on the hospital's staff. There, he served as ward chief and then as chief of the University service. (The hospital closed in 1977.) In 1979, he wrote a guide book for patients with M. F. Fox, *It's*

Your Body: Know What the Doctor Ordered – Your Complete Guide to Medical Testing. His many honors included the School of Medicine's Distinguished Graduate Award and the University's Alumni Award of Merit. He was asked by Penn's graduating medical students to be their commencement speaker in 1977 and again in 1982. In the 1990s, Schnabel turned his focus to care for the aging and became acting director of Penn's program in geriatric medicine and acting director of Penn's Institute on Aging. In 2001, the medical school established the William Maul Measey – Truman G. Schnabel Jr. Chair in Geriatric Medicine and Gerontology. A former president of the American College of Physicians, he received its Alfred E. Stengel Memorial Award.

Andrew Dickson Hunt, M.D., G.M.E. '43, East Lansing, Mich., a retired pediatrician; June 16, 2005. He had served as associate dean of Mercer University School of Medicine.

Morgan T. Milford, M.D. '44, Greenville, S.C., a retired surgeon; November 28, 2004.

Tom S. Mebane, M.D. '45, State College, Pa., a retired pediatrician and emergency medicine physician; September 21, 2008. He served as director of outpatient services at the Centre Community Hospital from 1970 until 1985.

Russell D. Squires, M.D. '45, G.M.E. '49, Sandy, Utah; February 11, 2009. He served in the Army Medical Corps in World War II. During the 1960s and '70s, he led physiological research at the Johnsville Naval Air Station in Willow Grove, Pa., studying among other things the gravitational effects on the first NASA astronauts.

Herman M. Panzer, M.D. '46, G.M.E. '52, Lafayette Hill, Pa., a retired dermatologist; March 11, 2009. He began a practice in 1946 in West Oak Lane. He later moved his office to Cedarbrook and was practicing in Chestnut Hill when he retired at 83. From 1959 to 1974, Panzer was chief of dermatology at Germantown Hospital.



F. Earl Fyke Jr., M.D. '47, Jackson, Miss., a retired medical director of Medical Assurance Co. of Mississippi; September 21, 2008. During the Korean War, he served as a U.S. Army medical officer in Korea.

Donald L. Mahler, M.D. '47, Newton Center, Mass., a retired anesthesiologist; January 18, 2009. He had been chief of anesthesiology at the Boston VA Hospital and professor of anesthesiologist at Tufts University School of Medicine.

Milton M. Heskell, M.D. '48, Abington, Pa., an endocrinologist in private practice who had also been chief of endocrinology at what is now Albert Einstein Medical Center; February 17, 2009. He completed his residency in endocrinology and diabetes at the Mayo Clinic and earned a master's degree in endocrinology at the University of Minnesota. After serving as a physician for coal-mining companies in Kentucky and West Virginia, he was an Air Force flight surgeon stationed in Florida and Texas.

Flora Herman Biele, M.D., G.M.E. '49, Brooklyn, N.Y., a retired psychiatrist; July 7, 2006.

Walter Brown Shelley, M.D., G.M.E. '49, Grand Rapids, Ohio, former professor and chair in the Department of Dermatology; January 30, 2009. He received his medical degree from the University of Minnesota and was appointed to Penn's standing faculty in 1950 after completing his residency at HUP. He taught and conducted research that resulted in the discovery of many diseases, including allergies to female hormones, and discovered a milk-like secretion of the armpit glands responsible for odor that led to the development of antiperspirant. In the 1960s, he devised a test to detect penicillin sensitivity, and in the 1970s, he pinpointed the cell causing an allergic reaction to poison ivy contact. He also introduced the use of Botox injections to control sweaty palms. Shelley served as chair of the Department of Dermatology from 1965 until he

resigned in 1980. After leaving Penn, he joined the faculty of the Medical College of Ohio (now the University of Toledo College of Medicine), and he retired there in 1997. He was the author or coauthor of 16 books and more than 600 scientific articles, including a major textbook, *Dermatology* (1956) and his autobiography, *The Skin Around Me: Adventures in Dermatology* (2007). During World War II, he served in the Army, researching how the body acclimatizes — and sweats — in tropical conditions. He served as president of five major American dermatologic organizations: the American Academy of Dermatology, the Society for Investigative Dermatology, the American Dermatologic Association, the American Board of Dermatology, and the Association of Professors of Dermatology. His honors included an honorary doctorate degree from Uppsala University, awarded by the king of Sweden.

Vernon A. Vix, M.D. '49, Nashville, Tenn., a retired professor of radiology at Indiana University; September 26, 2008. He did his internship at Tulane University and his residency at the University of Minnesota. He had also been a faculty member at Vanderbilt University School of Medicine. During the Korean War, he served as a U.S. Air Force medical officer in Alaska.

James H. Mason IV, M.D., G.M. '50, Ventnor, N.J., a retired surgeon; May 18, 2007. He served during both World War and the Korean War and received a Bronze Star. He was a former member of the clinical faculty at Hahnemann Medical College. He practiced surgery for more than four decades at the Atlantic City Medical Center, where he had also served as chief attending surgeon and surgical director. A former president of the Atlantic City Medical Society, he had been president of the United Way of Atlantic City.

Leon Aller, M.D. '51, Snohomish, Wash., a family doctor; October 14, 2008. At 17, he began training as an Army medic, and during World War II he saw combat service in the Pacific with the 41st Infantry Division. For

his service, he received the Silver Star and other military honors. After leaving Penn, Aller took his residency in family medicine in Washington and in 1953 opened a private practice. In 1962, he established the Snohomish Family Medical Center, a community outreach clinic. One of the clinic's goal was to send volunteer physicians to areas of the developing world where doctors and knowledge of modern medical technology were sorely needed. He also co-founded Job Therapy, a counseling and placement service for non-violent criminals, also in Snohomish. While serving as a clinical associate professor of family medicine from 1955 to 1994 and rising to surgeon general of the Washington National Guard, Aller also devoted himself to his medical missionary work. In that role, he worked in Africa, Papua New Guinea, the Middle East, and Latin America. He eventually concentrated his efforts on Guatemala, where he played a vital part in the construction of the first hospital for the town of Santa Cruz Barillas. The humanitarian organization he founded, Hands for Peacemaking Foundation, trains doctors, nurses, and lab technicians for service in the developing world. For his missionary work and many other efforts, Aller was named America's Family Physician of the Year by the American Academy of Family Physicians in 1987. He also served as president of the Washington Academy of Family Physicians.

Henry W. Allison, M.D., G.M. '52, Stow, Ohio; September 2, 2008. He served as chief of internal medicine at Akron City Hospital from 1960 to 1964 and was honored by the residents for outstanding teaching at the hospital. He also served as the hospital's chief of staff. A recipient of the Laureate Award from the American College of Physicians, he also received the Physician Recognition Award from the Summa Health System.

Guy E. Irvin, M.D., G.M.E. '52, Tazewell, Va.; October 10, 2004.

Lonnie W. Funderburg, M.D., G.M.E. '53, Birmingham, Ala.; March 13, 2009. He was an educator and founder of what is now Samford University's graduate program for nurse anesthesia. He served as an overseer of Samford University and was honored as *Alumnus of the Year* in 1998. He made several short-term medical mission trips to various countries.

Patricia F. Borns, M.D., G.M.E. '55, emeritus professor of radiology at Penn; April 15, 2009. She earned her M.D. degree from Women's Medical College in Philadelphia, where she was elected to Alpha Omega Alpha. Before coming to Penn, she had been at Thomas Jefferson University Hospital. She was promoted to associate professor of clinical radiology in Penn's School of Medicine in 1971. She left Penn to head the radiology departments at Hahnemann University Hospital and the Alfred I. DuPont Hospital for Children in Delaware. In the mid-1980s, she returned to Penn, at which time she was appointed professor of radiology at The Children's Hospital of Philadelphia. She was considered a pioneer in pediatric radiology: one of her findings was that some problems that arise during cancer treatment in children can be eliminated if doctors are aware of what side effects to expect for specific drugs.

Arthur Evans, M.D. '55, Santa Rosa, Calif.; March 10, 2009. He specialized in treating patients with arthritis and rheumatism.

Gerald A. Huestis, M.D., G.M. '56, Santa Ana, Calif., a former surgeon; December 24, 2004.

William Dorner Jr., M.D., G.M. '57, Akron, Ohio, July 14, 2008. He had been a dermatologist at the Cleveland Clinic and in private practice.

Francis A. Hurtubise, M.D., G.M. '57, Los Angeles; March 13, 2004.

Roshen N. Irani, M.D., G.M. '57, Philadelphia, Pa., a retired pediatric orthopaedic surgeon; June 5, 2007. She had been an adjunct associate professor at Thomas Jefferson University.

Robert E. Rowand, M.D., G.M.E. '57, Westfield N.J.; November 29, 2006. During the Korean Conflict, he worked with NATO and was assigned to Naples, Italy, and Turkey, to care for the military officers. Later, in New York City, he performed logistical work for the Navy, then ended his military career in Little Creek, Va. He also did pharmaceutical research for such companies as Lederle and DuPont and eventually retired from Ciba-Geigy. Rowand served as the president of the Summit Chapter of the American Red Cross and had been a staff physician at the Overlook Hospital in Summit.

John H. A. Bomberger, M.D., G.M.E. '58, Norristown, Pa., a retired pediatrician; December 14, 2002. For almost 30 years, he cared for children in his Drexel Hill office and was on the staff of Delaware County Memorial Hospital, where he became chief of family service. After retiring from his practice and from the hospital in 1989, he was medical director of Mirmont Center, a drug- and alcohol-rehabilitation facility in Lima.

Lily Ruckstuhl, M.D., G.M. '58, Fountain Hills, Ariz., a retired specialist in internal medicine; November 24, 2008.

H. Pierce Allgood, M.D., G.M. '59, Atlanta, a retired orthopaedic physician, affiliated with Piedmont and Kennestone hospitals; July 24, 2008.

William F. E. Hanby Jr., M.D. '59, Huntingdon Valley, Pa., a retired radiologist at Abington Memorial Hospital; September 16, 2008. He was a flight surgeon with the U.S. Air Force Strategic Air Command, 1961-63. In 1999, he was named Abington Memorial Hospital's "Physician of the Year."

Robert M. Rogers, M.D. '60, G.M. '66, Pittsburgh, September 4, 2008. The first full-time member of the pulmonary division at Penn, he founded the first respiratory intensive-care unit on the East Coast. From 1972 to 1980, he was at the University of Oklahoma, then joined the University of Pittsburgh, where he became

chief of pulmonary, allergy, and critical care medicine. To honor his distinguished service, Pitt established a lectureship in his name. Recipient of the Presidential Award of the American Thoracic Society, he also received the Special Recognition Award from the American College of Chest Physicians.

John G. Guillemont, M.D. '62, G.M.E. '67, Boston, a retired chief of pathology at Winchester Hospital; July 29, 2008.

Richard E. Shelling, M.D. '64, Sayre, Pa.; January 24, 2008. An internist and member of the Tioga County Health Department, he served as treasurer for the Bradford County Medical Society and was a diplomat of the American College of Physicians. He had been on the board of Carantouan Greenway, a conservation group.

Gary L. Enold, M.D., G.M.E. '61, Amsterdam, Ohio, a former surgeon; September 25, 2006.

John Lower Ickler, M.D., G.M.E. '62, Abington, Pa., a retired pediatrician; June 6, 2000. He had worked in the pediatrics department at Abington Memorial Hospital.

David B. Sloan Jr., M.D. '63, G.M.E. '67, Wilmington, N.C., a retired ophthalmologist; December 19, 2008. He served two years in Guam as a Naval physician during the Vietnam War. A former president of the New Hanover County Medical Society, he had been chief of staff of the New Hanover Regional Medical Center and chairman of the ophthalmology section of the North Carolina Medical Society. In 1975, he founded Eye Associates of Wilmington, Pa., with Dr. Frederick C. Butler and Dr. James B. Sloan.

John C. Bell, M.D. '67, Montgomeryville, Pa., a retired neurologist; January 25, 2009. In 1969, during the Vietnam War, he was drafted into the Army and was a doctor stationed at Tripler Army Medical Center, Honolulu; he was discharged as a major in 1971. He took his neurology residency at the University of Wisconsin, Madison, in 1975. Bell began his medical career at St. Joseph's Hospital before going into private

practice in Abington with his father. He was a consultant at several hospitals, including Chestnut Hill Hospital, and he worked in the clinic at Hahnemann Hospital. He retired from Roxborough Hospital in 2005 because of olivopontocerebellar atrophy, a rare neurological disease that eventually caused his death.

E. Ross Kyger, M.D. '67, G.M.E. '74, Houston, Texas; March 26, 2009. He received a training grant for future academic surgeons from the National Institutes of Health and in 1973 received the research award from the Central Pennsylvania College of Surgeons. A former associate professor of surgery at the University of Texas Medical School (Houston), he has been clinical associate professor of surgery there from 1978 until his death. His other appointments included chief of cardiovascular surgery and director of non-invasive vascular laboratories at St. Joseph Hospital in Houston. Kyger was honored by several organizations, including the Denton A. Cooley Cardiovascular Surgery Society. A fellow of the American College of Cardiology and of the American College of Surgeons, he served as the chairman of the Task Force on Hypertension of the Houston Heart Association and had been president of the association's executive committee. He served as president of the board of directors of the Texas Affiliate of the American Heart Association and president of the Houston Chapter of the American Heart Association.

Jack H. Weinstein, M.D., G.M.E. '70, a retired psychiatrist who treated patients at the Institute of Pennsylvania Hospital for more than 40 years; April 11, 2009. During World War II, he served in the Army Medical Corps and was later recalled to active duty during the Korean War and was stationed at Valley Forge Army Hospital in Phoenixville. A specialist in bipolar disorder, he was considered a pioneer in the use of medications to treat psychiatric disorders. He was also prominent in the movement to treat addictions as illnesses. From 1953 to 1954, Weinstein was clinical director of psychiatry at Phila-

delphia General Hospital. In the 1960s, he was on the staff of the Diagnostic Relocation Center, a facility to treat drug addiction and alcoholism.

Paul E. Epstein, M.D., G.M.E. '71, Gladwyne, Pa., former chief of pulmonary medicine at Penn Medicine at Radnor; March 12, 2009. He was co-editor of the Medical Knowledge Self-Assessment Program, a collection of booklets designed to educate internists, and had been associate editor and deputy editor of the *Annals of Internal Medicine*. In 1977, he was part of a Penn team that treated very sick patients with an experimental artificial-lung machine. Epstein was a clinical professor at the University of Pennsylvania School of Medicine and in 1973 became founding director of Penn's Cardiovascular Pulmonary Training Program. For 17 years, he was chief of the pulmonary division at Graduate Hospital, until 1999. He then served for eight years as chief of pulmonary medicine at Penn Medicine at Radnor. A specialist in occupational lung diseases, he was an examiner for the federal Black Lung Benefits Program. In 2005, he testified before the Senate Judiciary Committee at a hearing on asbestos and the Federal Employers' Liability Act. A former president of the Pennsylvania College of Internal Medicine, he was named a master of the American College of Physician.

John Ibach Jr., M.D., G.M.E. '79, Jacksonville, Fla., a former surgeon and jazz pianist; September 11, 2005. During the Vietnam War, he served in the U.S. Army Medical Corps, performing surgery in a field hospital. In Jacksonville, he joined the staff of Baptist Medical Center and became its chief of thoracic and cardiovascular surgery. He also served as clinical associate professor of surgery at the University of Florida. He had been president of the Florida Thoracic Society, the Florida Society of Thoracic and Cardiovascular Surgeons, and the Jacksonville Chapter of the American College of Surgeons. On the musical side, he was a director of the Delius Association, the St. John's River Band, and the Riverside Fine Arts Association. He



occasionally performed with jazz bands and recorded several CDs.

Faculty Deaths

Harry C. Bishop, M.D., Haverford, Pa., emeritus professor of surgery and retired senior surgeon at The Children's Hospital of Philadelphia; May 4, 2009. In his 37-year career as a pediatric surgeon, he operated on approximately 9,000 children and played a pivotal role in advancing what was then a young subspecialty by pioneering many surgical techniques. Before coming to Philadelphia, he received his M.D. degree from Harvard Medical School and was chief pediatric surgical resident at Children's Hospital, Boston. Bishop was recruited to Children's Hospital in 1954 by C. Everett Koop, M.D., G.M.E. '47, then the surgeon-in-chief. Together they pioneered the Bishop-Koop procedure, used to treat intestinal obstruction in babies with cystic fibrosis. Bishop helped define particular birth defects and developed diagnostic methods and operative techniques to save many newborns. In 1966, he was part of a team that cared for a baby girl born without a small intestine. Their groundbreaking work proved for the first time that human infants could survive and grow on hyperalimentation, a form of intravenous feeding. Bishop retired in 1991.

Paul E. Epstein, M.D. See Class of 1971.

Lionel A. Manson, Ph.D., a retired professor of microbiology and former faculty member at the Wistar Institute; April 1, 2009. He earned his Ph.D. degree in biological chemistry from Western Reserve University in 1949. He came to Penn in 1954 as a research assistant professor, and his research interests included immunological responses during progressive tumor.

Justin Ludgar Parr, M.D., Radnor, Pa., an adjunct faculty member in the Department of Pathology and Laboratory Medicine; March 27, 2009. A neuropathologist, he had served on the faculty of Hahnemann University in Philadelphia before joining Penn. He earned his medical degree

from the University of Wisconsin and completed residencies in anatomic and clinical pathology and in neurology at University Hospital in Cleveland. He had been part of a research team from Penn and the Thomas Jefferson University School of Medicine whose findings, published in 2006, may help in the development of an oral therapy for multiple sclerosis.

Robert M. Rogers, M.D. See Class of 1960.

Truman G. Schnabel, M.D. See Class of 1943.

Walter Brown Shelley, M.D. See Class of 1949.

Richard Spielman, Ph.D., the Butterworth Professor of Genetics and a renowned expert in the fields of human genetics and genomics; April 25, 2009. His seminal work with Warren Ewens, Ph.D., of Penn's biology department, on family-based genetic associations studies, the Transmission Disequilibrium Test, has had a major impact on the field. His more recent studies with Vivian Cheung, M.D., professor of pediatrics at The Children's Hospital of Philadelphia (and Dr. Spielman's wife), were the first to investigate the genetics of natural variation of gene expression in humans. Spielman was the founding chair of the Genomics and Computational Biology Graduate Group, which has become the model for similar programs elsewhere. He received his Ph.D. degree in human genetics from the University of Michigan. After completing his postdoctoral training at Michigan in 1974, he joined what was then the Department of Human Genetics at Penn. He served on the editorial boards of several prominent journals, including the *Journal of Clinical Investigation*, the *American Journal of Human Genetics*, and *Genome Research*. He was a member of several NIH study sections.

William R. Straughn Jr., Ph.D. '58, Chapel Hill, N.C.; December 8, 2005. An emeritus professor of at the University of North Carolina School of Medicine, he had earlier been a professor of bacteriology and immunology at Penn.

Stephen T. Whelan, M.D. See Class of 1940.



Heartfelt Appreciation Becomes Lasting Legacy



The Staller Family: Chad Staller (center) with his sister Shara Rich, and their father Jerome. Chad is holding his nephew, Bradley Rich.

Jerome Staller was always an innovator. An accomplished businessman with a doctorate in economics, he founded the Center for Forensic Economic Studies, one of the first consulting firms in the United States to focus on the analysis of damages and liability in civil litigation. He continued to break new ground in forensic economics and as a bestselling author.

When Mr. Staller needed treatment for a heart condition, he chose another innovator – Michael A. Acker, M.D., Penn's chief of cardiovascular surgery and one of the nation's top heart surgeons. The relationship between Dr. Acker and his patient was one of mutual admiration, according to Mr. Staller's son, Chad. In addition, the entire Staller family spent a great deal of time at Penn as Mr. Staller was undergoing treatment. In that time, they came to know Dr. Acker and the entire staff well, and appreciated the expertise and professionalism of everyone at Penn Medicine.

In gratitude for the care he received at Penn, Mr. Staller decided to make a planned gift to Penn Medicine through life insurance. He passed away in 2008.

"My father respected how everyone at Penn held themselves to the highest standards," said Chad. "He was himself a successful man and Dr. Acker is a superior surgeon. My father saw something good happening with Dr. Acker and his staff in the cardiac unit."

Naming Penn Medicine as a beneficiary of a life insurance policy is a wonderful way to incorporate Penn into your estate plans. Donating a fully paid-up life insurance policy can be an effective way to make a generous gift, reduce one's taxable estate, and receive a federal income tax deduction.

As you chart your financial future, the Office of Planned Giving is ready to assist in developing an appropriate strategy to incorporate your charitable objectives. Contact Christine S. Ewan, J.D., director of Planned Giving, at 215-898-9486 or at Penn Medicine, 3535 Market Street, Suite 750, Philadelphia, PA 19104-3309. You can e-mail Christine at cewan@upenn.edu. We also invite you to visit the new Web site at www.med.upenn.planyourlegacy.org.

Considering the Physician Workforce

In 2006, even before the current financial crisis, the Association of American Medical Colleges (AAMC) was concerned enough about a projected physician shortage that it called for a 30 percent increase in medical school enrollment. Last November, in a report called *The Complexities of Physician Supply and Demand: Projections Through 2025*, the AAMC restated the points it had raised over the last few years: a physician shortage already exists in parts of the country; almost one in three doctors in practice is 55 years old or older and likely to retire over the next 20 years; a growing population “may drive demand sharply upward for specialties that predominantly serve the elderly.” The report also mentions “mounting evidence of place- and specialty-specific shortages across the U.S.,” which I find one of the most persuasive observations. The physician supply is a longstanding issue, but as the nation considers reforming the health-care system, the topic has new urgency.

Based on current trends, the report posits a shortage between 124,000 and 159,300 FTE physicians by 2025. Either figure is challenging for the schools that prepare our future doctors. Still, as the word *complexities* suggests, such projections are not only complicated but open to debate. As the report states, “There is much work to be done to better understand the dynamics of the physician workforce.”

One important factor that influences career choices is the escalating cost of attending medical school. According to last year’s AAMC’s Graduate Questionnaire, students had an average debt load of more than \$140,000, and 17.7 percent of graduates carried educational loans of \$200,000 or more (*AAMC Reporter*, December 2008). Some experts argue that debt strongly influences which specialties new graduates select, often to the detriment of lower-paying specialties in primary care, and that the cost of medical school may limit underrepresented in medicine students from applying.



The Journal of the American Medical Association has also looked at factors influencing career choices. “Structural changes to the curriculum to facilitate more primary-care experiences promoted student interest in primary care, but [projected] income, debt, and work hours dissuaded students from this path. . . . Students increasingly prioritize life-style issues when choosing careers” (September 10, 2008). Based on my experiences at Penn Medicine and elsewhere, however, I believe most students still uphold the altruistic ideals of the profession. Every year, at numerous events involving our students, it is refreshingly clear that they retain a powerful civic impulse.

As leaders of our medical schools continue to monitor the physician workforce, we look to organizations like the AAMC and the Association of Academic Health Centers to help us. At Penn, we are fortunate to have one of the most respected experts on this issue in Richard A. Cooper, M.D. Dr. Cooper spent many years here, then served as dean and executive vice president at the Medical College of Wisconsin. He returned to Penn in 2005 as a professor of medicine and a senior fellow in the Leonard Davis Institute of Health Economics. He has studied the physician and nurse workforce for many years, and numerous articles acknowledge his work. Today, he is also co-chair of the Council on Physician and Nurse Supply, with Linda H. Aiken, Ph.D., R.N., the distinguished Penn professor of nursing and of sociology.

In May, Dr. Cooper testified before the United States Senate Committee on Health, Education, Labor, and Pensions. Any effort to reform the nation’s health-care system, he said, must deal with worsening shortages of physicians. The

fundamental problem, as he put it bluntly, is “too few physicians to serve the needs of the nation.” As he has in the past, he argued for expanding the number of medical students and, even more important, expanding residency programs. He also urged “innovative practice arrangements” among physicians, hospitals, and nonphysician clinician providers.

Even if the projections about the physician workforce are only partially correct, how should a school like ours respond? For a start, provide more financial aid. In 2005, we awarded \$4.9 million in financial aid to some 250 students – about a third of the total number of students enrolled in any one year. We want to do much more, which is why we set a goal of raising \$100 million for student financial aid, as part of Making History: The Campaign for Penn. Our most recent count was \$24 million raised. That’s very impressive, but we hope to reach our ambitious goal.

Our school regularly places in the top five among what *U.S. News & World Report* calls “research-oriented” medical schools. On the other hand, our school is also ranked – with less fanfare – among the schools more oriented toward primary care. In the last few years, our school has been ranked higher on that survey as well. In 2004, it was 46th, but this year it was 12th. Even in the research-oriented survey, Penn consistently ranks very high in internal medicine. In short, our excellent students have a wide range of career options before them.

We look to professional organizations and experts like Dr. Cooper to help us shape our policies on the physician workforce. At this point, we do not believe Penn Medicine should increase the size of its classes. Our goal is to continue to produce the future leaders of the profession, and it is in fulfilling that role that we believe we can serve the nation best. ■

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t Penn, a critical mass of experts and sophisticated new technologies has helped transform transfusion medicine. Although it continues its diagnostic function, transfusion medicine is increasingly involved in therapy – for example, in collecting and purifying lymphocytes that will be re-engineered to combat specific infections or attack cancer cells.