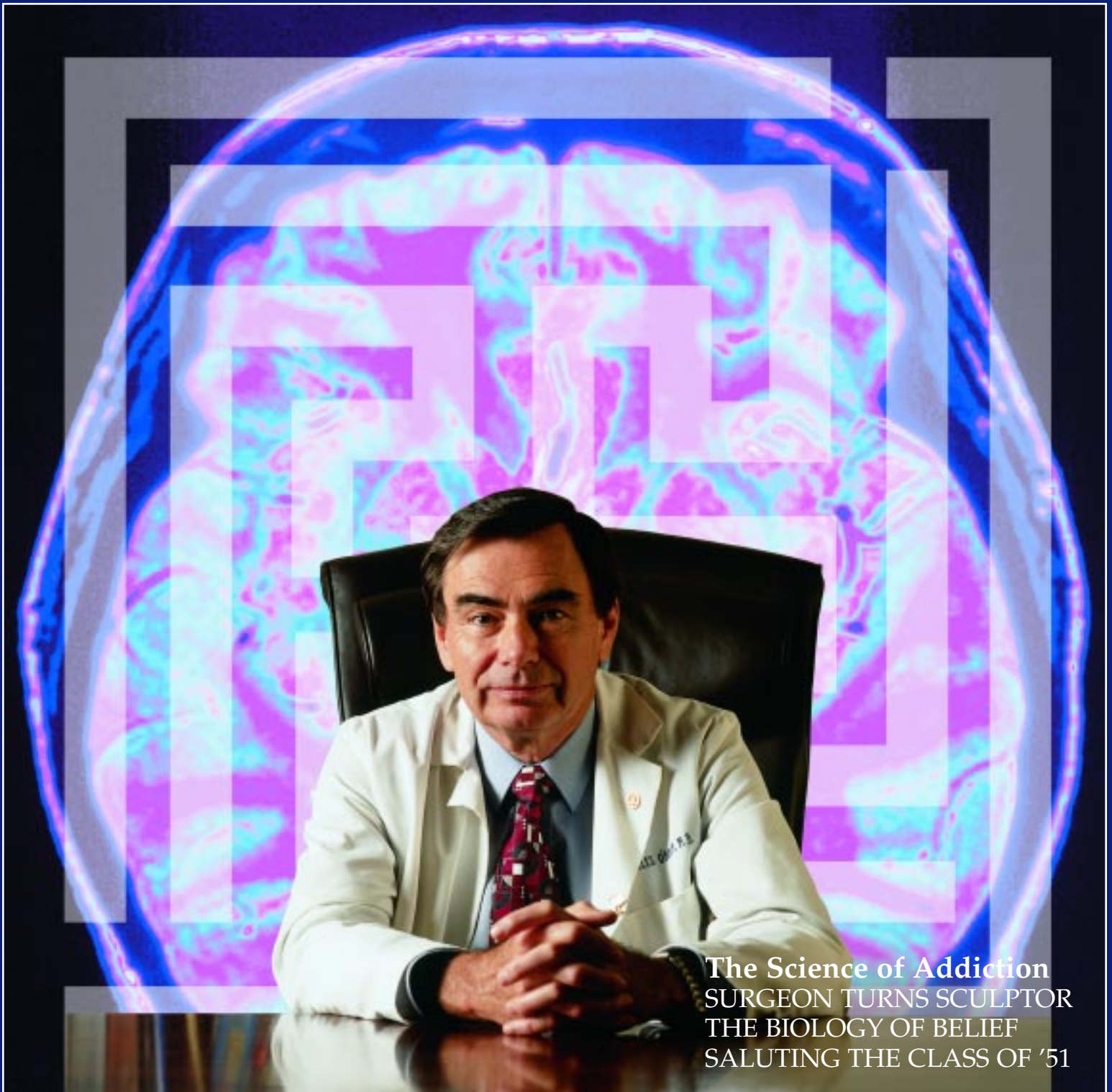


# PENN MEDICINE

UNIVERSITY OF PENNSYLVANIA MEDICAL CENTER ■ SUMMER 2001



**The Science of Addiction**  
SURGEON TURNS SCULPTOR  
THE BIOLOGY OF BELIEF  
SALUTING THE CLASS OF '51

### Saluting Bill Kelley

This spring, the School of Medicine held a symposium in honor of William N. Kelley, M.D., who served for more than 10 years as dean of the school and CEO of Penn's Health System. "Predictions for the Next Millennium" was moderated by Edward W. Holmes Jr., M.D. '67, vice chancellor for health sciences and dean of the School of Medicine at the University of California at San Diego. (Holmes chaired Penn's Department of Medicine from 1991-97, recruited by Kelley.) Describing the guest of honor as "one of the dominant figures in American medicine," Holmes asserted that Kelley had "transformed the School of Medicine." Kelley, he said, worked to make it possible to translate fundamental discoveries more quickly into patient care; mandated an innovative curriculum; encouraged one of the premier M.D./Ph.D. programs in the country; and increased Penn's NIH research funding until it was second among all medical schools. As dean, Kelley recruited 20 department chairs – and made it possible to attract the very best medical students. At the symposium, several prominent friends and colleagues spoke on topics central to Kelley's vision of an integrated academic health system. Following are some brief highlights.

Samuel O. Thier, M.D., president and CEO of Partners HealthCare System in Boston, spoke about academic health centers as "ground zero for change in health policy." He noted that in the 1990s, funding from the NIH rose to unprecedented levels – while reimbursements from insurance companies and Medicare went down. Simultaneously, the burden of uncompensated care for AHCs grew heavier. It is clear, said Thier, that the old way of organizing a medical center "is no longer viable."

In general, Thier argued, academe has the important role of contributing ideas and models for public discourse. Academic health centers should "ask the questions properly and toughly" and "make sure the debates are better informed" than they often are.

Holmes introduced Gail Morrison, M.D. '71, Penn's vice dean for education, as "the chief architect of the new curriculum." Morrison listed several challenges the curriculum must face. The explosion of new knowledge forces medical schools to reassess what needs to be taught and learned. The curriculum must allow different ways of "keeping up" and encourage students to be self-directed learners, often by using the newest technologies. Morrison recalled that Kelley had charged her with "a fundamental restructuring" of medical education. One part of that vision, she said, remains elusive: making it more affordable.

P. Roy Vagelos, M.D., former chairman and CEO of Merck and former chairman of the University trustees, sketched out the great advantages when the universities do the basic research, the government bears part of the cost, and industry does the rest of the "discovery" work. He cited three areas in which such productive partnerships had benefited patients tremendously: coronary heart disease, hepatitis B, and benign prostate enlargement.

Among the issues raised by Kenneth I. Shine, M.D., president of the Institute of Medicine of the National Academy of Sciences, was quality of care. Medical institutions, he asserted, had lost leadership and credibility in the eyes of the policy makers, nor had they done a good job in providing access to care. Quality, he said, "represents the last remaining area" where medicine can take the lead and convince the public that it is doing so for the public's benefit. For that, however, medical institutions will need accurate measurements, which they have not had.

Shine also praised interdisciplinary research. Yet, he said, "from a policy point of view, we keep subdividing and subdividing and subdividing," and the way research is currently funded does not help interdisciplinary study. He ended his remarks by raising a related "central issue": the growth of systems of care

involving multiple health professionals. Because a variety of disciplines and competencies come into play, he suggested that the various health professionals be educated together. In fact, he feels it would be beneficial to have them problem-solve as teams while in training. Like Morrison, he emphasized that people must be educated not just for life-long learning but for change as well.

Francis S. Collins, M.D., Ph.D., director of the National Human Genome Research Institute, was recruited to the University of Michigan by Kelley when Kelley was chair of its Department of Internal Medicine. Collins spoke about the impact of the human genome project and predicted how the future was "all going to play out." By 2010, he envisioned predictive genetic tests for perhaps a dozen risks; preimplantation diagnosis will be widely available (although the limits of the process will be "fiercely debated"); and the federal government will pass effective legislation against genetic discrimination. By 2020, there will be gene-based designer drugs on the market for diabetes, hypertension, and several other conditions. Cancer therapies will improve significantly.

By 2030, comprehensive genomics-based health care will be the norm. Individualized preventive medicine will be available. For many diseases, the interaction of environmental factors with the human genotype will be pinpointed. A full computer model of the human cell will replace many laboratory experiments. The average life span will reach 90 years; even so, major anti-technology movements will arise. Finally, there will be serious debate about humans possibly "taking charge" of their evolution.

Following the symposium, the visionary gave way to the pictorial. After several speakers gave remarks, a portrait of the guest of honor was unveiled. The portrait now hangs in Biomedical Research Building II/III, constructed during Kelley's tenure – and one of the most visible signs of his ambitious plans for Penn's medical school and Health System.



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Robert Clink

Arthur H. Rubenstein, M.B., B. Ch., will lead Penn Med.

## Mount Sinai's Rubenstein is named new EVP, dean

Arthur H. Rubenstein, M.B., B.Ch., an accomplished physician, internationally known endocrinologist, and leader in academic medicine, has been named executive vice president of the University of Pennsylvania for the Health System and dean of the School of Medicine. Rubenstein, 63, has served for the past four years as dean and Gustave L. Levy Distinguished Professor at Mount Sinai School of Medicine in New York. As dean, he is credited with recruiting and retaining outstanding faculty, developing and implementing a comprehensive strategic planning process, and leading a successful effort to increase the school's federal funding for research. Before going to Mount Sinai, Rubenstein was on the medical faculty of the University of Chicago for 30 years and served as chairman of its Department of Medicine from 1981 on.

Speaking at a campus press conference, Rubenstein called the Penn position "a job made in heaven for me." As he put it, "I love universities, I love academic medicine." He underscored the importance of close ties between a university and its hospitals. While he plans to make sure that Penn is strong in all the major clinical areas that attract patients, Rubenstein also emphasized that treatments at Penn will be at the cutting edge, "where research intersects patient care."

As executive vice president, Rubenstein will report to Judith Rodin, Ph.D., president of the University of Pennsylvania; as dean, he will report to Robert Barchi, M.D., Ph.D., the provost (the University's chief academic officer). Robert D. Martin, Ph.D., CEO of the Health System, will report to Rubenstein.

Barchi praised Rubenstein's "years of experience and a keen appreciation for the challenges facing today's academic health systems." The ultimate structure of the Health System and its relationship with the School of Medicine have not been decided, but Rubenstein suggested that the components would be closely aligned. "I'm going to work with my colleagues in the Medical Center, with Dr. Rodin, with the board, to try to find exactly the right structure over the next several months," he said. At the same time, Rubenstein emphasized the need to make sure that "the Health System and the medical school conglomerations don't negatively impact a great university" because of the volatility of the health-care marketplace.

Author of more than 350 publications, Rubenstein is recognized for his expertise and groundbreaking research in diabetes. He is a member of the Institute of Medicine of the National Academy of Sciences and a fellow of the American Association for the Advancement of Science and of the American Academy of Arts & Sciences. Former president of the Associa-

tion of American Physicians and of the Association of Professors of Medicine, he has also been chairman of the American Board of Internal Medicine.

Born in South Africa, Rubenstein received his medical degree from the University of the Witwatersrand in Johannesburg in 1960. After affiliations with Witwatersrand, Johannesburg General Hospital, and the Hammersmith Hospital in London, he joined the University of Chicago in 1967.

As he made clear at his campus press conference, Rubenstein has devoted himself to all three components of academic medicine: education, research, and patient care. When asked whether he expected to be able to teach at Penn, he replied, "I wouldn't come if I couldn't teach. . . . It's in my bones and blood, and that's why I love universities." As he put it, "What keeps the faculty energized and on their toes and interested are outstanding students." He has taught values in medicine and noted that he is a "devotee" of William Osler. He feels it is extremely important to talk about values in medicine "at a time when we're really buffeted by all these difficult financial and HMO pressures and restricted time slots for patients." Equally important is the responsibility to "set the tone for young physicians to do what's right."

Rubenstein explained that he gave up research when he felt he was no longer "competitive" because of his administrative responsibilities. Even as chairman of medicine at the University of Chicago, however, he took care of patients, and he said he was "thinking seriously about starting again."

While noting Penn's various and often well-publicized strengths, Rubenstein mentioned what he called "an incredibly key issue." That was the faith the faculty showed in the institution, despite "this tremendously traumatic time" of financial constraints and uncertainty. "Almost to a person," he said, the faculty members he spoke with told him "we all believe so much in the place."

John Shea

## Health System continues its financial recovery

Although the final audited figures for Fiscal Year 2001 are not yet available, the University of Pennsylvania Health System continues to make progress in its financial recovery. Through the third quarter, ending March 31, 2001, UPHS had an operating profit of \$24.0 million. That is a \$34.8 million improvement over the corresponding period of the previous fiscal year. Given the Health System's recent history – when it had close to \$300 million in operating losses in FY1998 and 1999 – its showing for this current fiscal year appears all the more impressive. Nor has it gone unnoticed by Penn's peer institutions, the bond-rating agencies, and the media. For example, in the February 5 cover story of *Modern Healthcare*, the performance by UPHS was characterized as a "dramatic success" story.

Arthur Rubenstein, M.B., B.Ch., the newly named executive vice president for the Health System and dean of the School of Medicine, praised the "outstanding job" done by Robert D. Martin, Ph.D., the CEO of the Health System. Said Rubenstein, "The turnaround has been amazing – truly amazing."

## Gene therapy reverses blindness in dogs

Researchers at Penn's Scheie Eye Institute have developed a gene therapy protocol that successfully restored sight in dogs afflicted with a variation of Leber congenital amaurosis (LCA), a severe form of retinal degeneration that, in humans, renders infants permanently blind. The work was done in collaboration with researchers from Cornell University (who discovered the mutated gene in dogs) and the University of Florida (who helped establish the adeno-associated virus that served to deliver the necessary protein). The study

appeared in the May issue of *Nature Genetics*.

Under optimum conditions, normal protein transports a Vitamin A-like compound to the retina, which is necessary for sight. In some cases of animal and human LCA, wild-type RPE65 – the protein that transports the necessary Vitamin A-like compound – is missing from the gene, which results in blindness.

According to Jean Bennett, M.D., Ph.D., associate professor of ophthalmology and a senior co-author of the study, previous studies to reverse blindness in rodents have been successful, but this is



Jean Bennett, M.D., Ph. D.

the first successful outcome using larger animals. "This study takes a great stride forward in demonstrating that gene therapy does not just slow down a retinal degenerative disease, but can actually provide recovery of vision to an animal that was previously blind," said Bennett, a researcher at the F. M. Kirby Center for Molecular Ophthalmology at the Scheie Eye Institute.

In the Penn study, researchers injected a recombinant adeno-associated virus (AAV) carrying wild-type RPE65 into the area between the photoreceptors and the retinal pigment epithelium of three dogs. After 90 days, an electroretinogram showed that the waveforms of the treated eye were similar in scope to those of a sighted dog's eyes. Behavioral testing four months later was consistent with the electrophysiological results. The treated dogs all avoided collision with objects in front and to the right (the side injected), yet they consistently collided with objects to the left. In contrast, the untreated dog did not avoid objects in any direction.

Albert M. Maguire, M.D., associate professor of ophthalmology and one of the co-authors of the study, told *The Philadelphia Inquirer* that a few early experiments had attempted to inject the protein directly into the eye. These met with marginal success, however, and a better strategy seemed to be to administer the gene that would allow the dogs to make the protein themselves – which is the essence of gene therapy.

Since the publication of the study and its resulting publicity, Bennett has received hundreds of calls and e-mails. She cautions that "we are nowhere near the introduction of the missing protein in humans to restore sight," yet she is very optimistic about future developments.

The other researchers in the study are Samuel Jacobson, M.D., Ph.D. (Penn), Gregory Acland, V.M.D., and Gustavo Aguirre, V.M.D., Ph.D. (Cornell), and William Hauswirth, Ph.D. (Florida).  
*Rosann G. Thompson*

## Honoring Excellence

begun in the spring of 1997, the Awards of Excellence program is a way for the School of Medicine to recognize its most outstanding faculty members for their research and clinical achievements. This year's Awards of Excellence dinner is scheduled for Thursday, November 15, at 6:00 p.m., in the lobby of Biomedical Research Building II/III. Tickets are \$90.00. For more information or to attend, call Medical Alumni Relations at 215-898-5298.



Greene

Eberwine

## A new tool for the era of proteomics

Now that scientists have identified the genes in the human genome, the growing field of proteomics will provide descriptions of how the proteins encoded in those genes work. Researchers at Penn's School of Medicine have created the first new technology for the proteomic era, a technique sensitive enough to detect individual proteins and robust enough to screen hundreds or thousands of molecules in mass automation.

The technique is called IDAT (Immuno-Detection Amplified by T7 RNA polymerase). It has a variety of potential uses, from detecting cancer earlier to sifting through samples of molecules to find new candidates for drug research. In the 23 April 2001 edition of *Proceedings of the National Academy of Science*, the researchers described how they used IDAT to identify a protein marker for breast cancer at a resolution up to nine orders of magnitude more powerful than conventional techniques and explained how the technique can be further refined.

"IDAT can detect proteins earlier, faster, and with more sensitivity than other methods," said James H. Eberwine, M.D., professor of pharmacology and of psychiatry and one of the authors of the study. "Tumors, for example, often shed particular proteins at an early stage and the sooner you can detect the proteins, the sooner you can treat the cancer."

According to Mark I. Greene, M.D., Ph.D., professor of pathology and laboratory medicine, another of the study's authors, "IDAT has the potential to do for proteomics what PCR [polymerase chain reaction] did for genomics in the last two decades."

Not only can IDAT quantify the amount of protein – it is sensitive enough to pick out even a few copies of a protein out of a highly diluted sample. Moreover, IDAT does not rely on radioactive labeling and is far less time consuming and cumbersome than existing techniques.

Eberwine and Greene worked with colleagues Hong-Tao Zhang, Ph.D., Janet Estee Kacharina, and Kevin Miyashiro to develop the IDAT technique and further refine it for broader applications. They have also found a way to create universal detection molecules, so that IDAT could detect an unlimited variety of proteins as well as lipids, sugars, and other cellular molecules. The research that developed IDAT has been funded by the National Institutes of Health and the Leonard and Madlyn Abramson Family Cancer Research Institute at the University of Pennsylvania Cancer Center.

Greg Lester

### A tribute to Penn's women

Scheduled for November 1-2, "125 Years of Women at Penn" will include a ceremony honoring women "firsts" at the University, as well as book signings, talks, and panel discussions. One discussion is the medically oriented "Our Bodies, Ourselves: What You Know May Make the Difference." The registration fee for the two-day package of events is \$125. For more information, go to the event's website, [www.alumni.upenn.edu/celebratewomen](http://www.alumni.upenn.edu/celebratewomen), or call the University's Office of Alumni Affairs at 215-898-7811.

## LETTERS

### THE EARLY YEARS

I was a member of the inaugural "Bridging the Gaps" summer program for Penn Med students interested in community health in 1991. During that summer, I was able to establish the UCHC medical clinic that was featured in your Spring 2001 issue ["Clinical Care," by Marie Gehret]. My heart was filled with pride to see the clinic featured so prominently and to learn that it had met and exceeded our expectations since its inception. I moved to Seattle for residency and fellowship training but have run into enough Penn Med students through the years to know that the clinic was still in operation. However, the clinic's growth over ten years is remarkable and reflects greatly on the commitment of Penn Med students to serve and contribute positively to their community. The support of faculty, UCHC, and St. Agatha-St. James are essential to the clinic, but the students' commitment and sacrifice for the clinic is the life force that has kept the clinic alive.

I wanted to add some details about the early years that highlight the tiny events that, when pieced together over ten years, lead to the clinic as it exists today. First, without the initiative of students and faculty in the year before 1991, I would never have had the opportunity to commit a summer to establishing the clinic. Dr. Jerry Johnson [G.M.E. '79] was my faculty advisor in the summer of 1991. He gave me tremendous insight into the support needed to provide medical care and established a precedent that care was to be of the highest quality, regardless of the limitations of time, space, and money. We started with BP screening but were quickly confronted with the need for resources for drug treatment, STDs, simple medications, and occasional emergency care. Without Dr. Johnson's mentorship, the clinic would never have received approval to operate. In addition, Father Anthony Gonzales was a remarkable man who risked much of himself and his church to allow a group of naive

first-year medical students to come under his roof during a soup kitchen to provide medical care. Father Gonzales died in 1992 and I hoped the clinic would bear his name. As the students, faculty, UCHC volunteers, and clergy have changed with time, his name appears to have been lost. Finally, there were community health workers, undergraduate volunteers, and many of my classmates and friends who played vital roles in the clinic's early days. Without their contributions, the clinic would never have lasted past the summer of 1991.

When we started the clinic, we had visions of it becoming both a community resource and an educational experience for students, perhaps integrated with the medical school curriculum. I agree wholeheartedly with the sentiments in Marie Gehret's article that introducing students to this population in this setting early in medical school has very positive influences on their attitudes, clinical skills, and interpersonal skills. The clinic influenced the person and doctor I have become and provided the kind of care and education that my classmates and I sought when entering medical school.

In the first year we knew there wasn't time to accomplish all that we hoped but were elated to know that other students would follow, adding their own initiative to the clinic. It is extremely gratifying to see that the clinic has matured to be everything we dreamed and more, and that there is consistent faculty support to keep the clinic running. I want to applaud the hundreds of students and faculty volunteers who have individually and collectively contributed to something very unique for a community in desperate need of support. Well done. I am very proud of my Penn Med heritage and the legacy you have left for others to follow.

*David A. Kregenow, M.D. '95  
Fellow, Pulmonary and Critical Care  
University of Washington*

## BACK IN 1755

Neither your article or another one I read recently, perhaps in a Jefferson publication, mentioned the most fasci-

nating item at Pennsylvania Hospital.

Protected by a wooden cover is the original cornerstone which speaks of the beneficence of George III in supporting the new hospital. I do not recall the exact text but it would certainly be worth publication all these years later.

*Bernadine Z. Paulshock, M.D. '51  
Wilmington, Del.*

*The editor replies:* The timeline for Pennsylvania Hospital that is found on the hospital's website notes that the original cornerstone can still be viewed at the southeast corner of the East wing of the Pine Building. Instead of a wooden cover, it is now protected by a more contemporary Plexiglas cover. The text, drafted by Benjamin Franklin, acknowledges George II, who reigned until 1760. The text reads: "IN THE YEAR OF CHRIST MDCCLV. GEORGE THE SECOND HAPPILY REIGNING (FOR HE SOUGHT THE HAPPINESS OF HIS PEOPLE) PHILADELPHIA FLOURISHING (FOR ITS INHABITANTS WERE PUBLICK SPIRITED) THIS BUILDING BY THE BOUNTY OF THE GOVERNMENT, AND OF MANY PRIVATE PERSONS, WAS PIOUSLY FOUND-ED FOR THE RELIEF OF THE SICK AND MISERABLE; MAY THE GOD OF MERCIES BLESS THIS UNDERTAKING."

## TRUTH VS. TRADITION?

Re: "The First Turns 250" (Spring 2001): As a Penn graduate (x 3) and as one who spent ten years in Philadelphia, I am well aware of the importance of The Pennsylvania Hospital and of colonial dates and events in the background of the city.

As a native of Louisiana, and as one who has spent his entire post-residency career in Louisiana, I have some pride in this state, also, and a wish that historical accuracy be acknowledged.

Charity Hospital of Louisiana at New Orleans was founded in 1736 and celebrated its 250th anniversary with great fanfare in 1986. Thus I take exception to part of the opening sentence which credits Pennsylvania Hospital as "the oldest hospital in the United States." As "the

colonies' first hospital" – no question. But since Louisiana became part of the Union in 1812, the facts have been different for 189 years!

Let truth top tradition!

*Isidore Cohn Jr., M.D. '45  
Chairman Emeritus,  
Department of Surgery  
Louisiana State University*

*The editor replies:* Dr. Cohn's letter raises again the question of primacy, which we visited briefly in our Summer 2000 issue when trying to determine which was the oldest hospital constructed by a medical school for teaching purposes (Editor's Note: "Who Was First?"). Sources at Pennsylvania Hospital remain comfortable characterizing it as "the nation's first." The phrasing that troubled Dr. Cohn – "the oldest hospital in the United States" – is ambiguous, and was written perhaps too carelessly by me, not by writers at Pennsylvania Hospital. Yet "United States" is synonymous with "the nation," a political entity, rather than with "America," a geographic entity. One could argue, then, that Pennsylvania Hospital has been a United States hospital for 225 years and that Charity Hospital has been one for 189 years.

But whether Dr. Cohn is persuaded by this argument, the picture seems even more complicated than that. While conducting a search on the Internet, I discovered other claimants to the title of oldest hospital. In the San Francisco area, there is the Hospital San Juan of God, previously known as Saint John the Baptist Hospital. Its claim: founded in 1550. (As the web page oddly puts it, "Being also the oldest hospital in America that works in the same building of their foundation.") The site for Bellevue Hospital in New York calls it "America's oldest public hospital, which opened in 1736." (Compare the ushistory.org description of Pennsylvania Hospital as "America's oldest hospital.") If we define America as North America, there is also a claimant in Quebec: the Hôtel-Dieu du Précieux Sang, founded in 1637, "the oldest hospital in North America."

Taking the easy way out, the editor reserves judgment.

THE SCIENCE OF

# Addiction

By Lisa J. Bain





INVESTIGATORS IN **PENN'S DEPARTMENT OF PSYCHIATRY** ARE TACKLING THE COMPLEX AND OBSTINATE PROBLEM OF **ADDICTION** FROM A VARIETY OF ANGLES. THEIR APPROACHES INCLUDE FINDING **THE MOST EFFECTIVE DRUG TO DEADEN THE CRAVING**, SEEKING TO UNDERSTAND THE NEUROANATOMY OF MEMORY AND DESIRE, AND STUDYING THE **GENETIC LIKELIHOOD THAT AN INDIVIDUAL WILL BECOME ADDICTED**.

**T**he history of treatment for drug addiction has been a story of change and resistance to change. So says Charles P. O'Brien, M.D., G.M.E. '69, Ph.D., professor of psychiatry at Penn. As director of Penn's Treatment Research Center (TRC) since its founding in 1971, O'Brien has been a primary agent of that change. During his two years of service in the U.S. Navy during the Vietnam War, he treated soldiers returning to the States for a variety of illnesses, including many cases of heroin addiction. But he found no effective treatment to offer these veterans. Given his training in both neurology and psychiatry, O'Brien became particularly interested in the effect of drugs on the brain.

"While I was in the Navy, I used my own money and my Navy uniform and went around the country looking at the various programs that were in operation at the time," he says, noting that the uniform allowed him to travel at reduced fares around the country. The results of his quest were discouraging. There was little research being done and little knowledge among clinicians that any research was under way. "So we designed a program that would have treatment and research together, so that we could study the treatment in an organized way and try to find out whether treatment A was better than treatment B."

Federal funding was available because of the Vietnam War. "There was a tremendous hysteria about heroin addicts coming back to the United States," says

O'Brien. "That put a lot of pressure on us to develop treatment programs very rapidly." At that time, the focus was on heroin addiction; cocaine was then very expensive and not widely available. But in the 1980s, the cost of cocaine dropped and crack cocaine became available, which allowed more efficient delivery of the drug to the brain. As the demographics of drug use changed, so did the TRC, not only in terms of what was treated, but how it was treated.

Throughout the decade of the '70s, psychotherapy was the only available therapy and the results were not encouraging. In the mid '70s, O'Brien and colleagues demonstrated for the first time that drug effects were conditioned, and studies began to focus increasingly on using medication to treat addiction. This trend in research continues today, despite continued resistance among many of those delivering treatment. Meanwhile, research into the neurochemistry, neurophysiology, and genetics of drug addiction has changed the way scientists understand addiction and has led to a new generation of drug treatments.

Today, O'Brien oversees addiction research and treatment involving about 40 investigators at three main clinical sites – the TRC at Penn, Presbyterian Medical Center, and the Veterans Affairs Medical Center – as well as a network of affiliates throughout the Delaware Valley where clinical trials are conducted. Everyone treated at the TRC participates in a grant-funded clinical trial. Most of the funding comes from the

National Institutes of Health, and most of these trials are for the treatment of addiction to cocaine, alcohol, and nicotine.

#### **Animal models reveal clues**

One of the factors that has fueled the study of the science of addiction is the availability of animal models. In the late '70s, Joseph R. Volpicelli, then an M.D./Ph.D. student at Penn, was interested in using animal models of psychopathology to study the relationship between stress and medical problems, particularly addiction. One question he pursued: Might stress somehow cause people to become addicted? Using foot shock to induce stress in rats, Volpicelli observed the effect of stress on the animals' drinking behavior. "I was really surprised at the findings," he recalls. "What I found was that rats drink alcohol not when they are really stressed, but after the stress is over. It was that finding that led me to reexamine the whole relationship between stress and drinking and why some people become alcoholics."

In response to trauma, the body releases endogenous opiates called endorphins, naturally occurring brain chemicals that bind to opiate receptors in the brain. Binding of the receptors, whether by endorphins or by opiate-containing drugs such as heroin, stimulates the brain's "pleasure centers." Volpicelli theorized that when the stress is over the opiate level falls, resulting in an experience of let-down or withdrawal, and that alcohol stimulates the opiate receptors and compensates for the rebound withdrawal.

At about that time, Charles O'Brien was investigating the effectiveness of an opiate-receptor blocker called naltrexone for the treatment of heroin addiction. Volpicelli gave some of the naltrexone to his rats. "What I found was that you could block alcohol drinking in rats by blocking the opiate receptors," he says. In 1981, he completed the study, his dissertation, and earned his degrees, but the scientific community was slow to accept the idea that opiate receptors were involved in alcohol preference. "At that point when I was submitting papers, the reviewers would say things like, 'This person knows nothing about alcoholism, obviously he's really naive, and this theory is full of holes,'" recalls Volpicelli. "I saw some of the reviews and I was just getting killed, it was such a radical idea. But there's a part of me that sort of prays to the saint of lost causes, and that's part of why I got involved with alcohol research. Because people told me that you can't really treat alcoholics or you can't develop animal models of alcohol drinking – and when people would say I can't do something, that would get me motivated to show that you could."

In the mid '80s, Volpicelli began to conduct research in humans who were addicted to alcohol. In a double-blind study, he randomly sorted chronic alcoholics into two groups. After both groups went through detoxification, both also received psychotherapy. The difference was that one group received naltrexone and the other a placebo. "What we found was that people on naltrexone had much lower relapse rates than people who got the placebo," says Volpicelli.

Again his finding met with resistance. According to O'Brien, people did not believe the data. "It was too good to be true, but it was true," he says. Despite the opposition, "Joe wouldn't take no for an answer." When an independent research group from Yale repeated the study and got similar results, however, the scientific community

finally began to take notice.

Today, Volpicelli points out, the idea that opioids play a role in alcohol consumption is accepted in the research community, but translation into clinical practice continues to meet with resistance. Many people are against using a drug to treat addiction. They also view naltrexone as an insufficient approach to the problem of alcohol addiction: although it removes the "high" from drinking, it does nothing about what many people see as the root cause of alcoholism – a "character defect."

But Volpicelli, today associate professor of psychiatry at Penn, believes naltrexone *does* get at the root of the problem. "Some people, for reasons that are not their fault, when they drink alcohol their brain releases a lot of these endogenous opiates. So it produces a nice high, which is fine, except when you stop drinking you go through a rebound phase

where you want to redose. So naltrexone really gets at the core of what makes alcohol addictive – the tendency for one drink to set the occasion for the next drink."

Although the results of the first naltrexone study were impressive, over time Volpicelli and others observed that people stopped taking the medication because they missed the high. "An important limitation of this whole endeavor," he says, "is that you need to have the person motivated enough to take the medicine and want to get better for the medicine to work." For their second naltrexone study, he and his colleagues designed a more personal psychosocial treatment, which he calls the "BRENDA" approach, to be used in conjunction with naltrexone. "It's a more expensive approach but we think that since the results are so much better, it's ultimately cheaper in the long run for society and even for insurance companies." As

## Training Doctors to Treat Substance Abuse

Resistance to the idea that addiction is a chronic disease runs strong in American society. Nowhere is this more true than among medical professionals, according to Charles O'Brien, M.D., Ph.D. "People in practice practice the way they were trained," he says. And what medical professionals in training are learning, he adds, is "very, very little."

According to a survey conducted by the American Association of Medical Colleges (AAMC) in 1999-2000, only 5 of the 125 responding medical schools require a course in substance abuse. Most medical schools offer an elective or fold substance abuse studies into another required or elective course. At Penn, medical students are required to take a full course in addiction: 25 hours in the "brain and behavior" block of integrated neuroscience. One of the few such offerings across the country, it attracts students from other medical schools who come to

Penn to take the course, spend time at the TRC, and learn more about addiction.

The course evolved gradually over the past 30 years. In the early 1970s, O'Brien recalls, a group of medical students approached him and said they would like to learn more about addiction. At that time, drug reactions were common on college campuses such as Penn, and a volunteer group of medical students made themselves available to talk to troubled undergraduates about their drug problems. But the "student doctors" did not know very much, so they asked O'Brien to teach them. The elective course O'Brien set up was very popular with students — "standing room only," as he puts it.

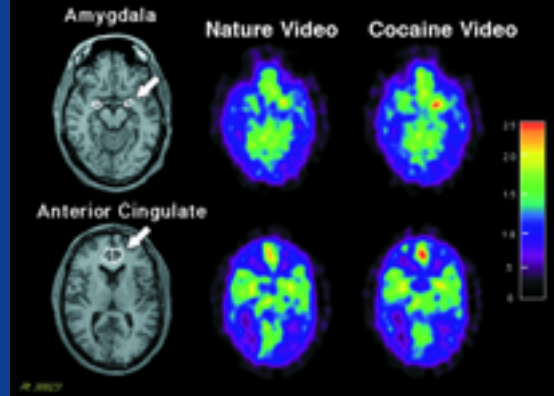
Then, in the late '80s, the School of Medicine held a retreat to review the curriculum and invited several recent graduates of the school to talk to the faculty about what they felt they had missed in their training. Says O'Brien, "One

the people get better, the treatment “keeps them out of hospitals, out of emergency rooms, out of needing liver transplants.”

In a third study, the team showed that the treatment could be delivered by nurse practitioners. More importantly, they showed that treatment over nine months rather than three months yielded better results. “It’s like the treatment of hypertension, diabetes, or asthma,” says Volpicelli. “You stop the medication and people’s symptoms come back. So it looks like alcoholism is like other chronic medical diseases in which you need long-term care as opposed to just going away for 30 days and expecting that people are going to get better.”

**The neuroanatomy of desire**

The pleasure centers of the brain that are tickled by alcohol are, of course, also activated by a host of other stimuli, from food



Courtesy of Anna Rose Childress, Ph.D.

and sex to cocaine and heroin. The centers are located in the limbic regions of the brain, which devel-

oped early in human evolution and have functions related to activities important to survival – eating, reproducing, and avoiding danger. Animal studies have identified certain areas in the brain that are especially important in this circuit. One of these is a small almond-shaped structure called the amygdala, found in the middle part of the temporal lobe of the brain. This is a “way station” that is critical for learning about reward or danger. Another structure involved in the circuit is called the anterior cingulate, which appears to be important in riveted attention and emotional reactivity. The amygdala, the anterior cingulate, and a third structure called the nucleus accumbens are part of a circuit that, says Anna Rose Childress, Ph.D., “enables the organism not just to experience the reward, the pleasure, or the danger, but to learn about it, so that they can get back to what they perceive to be the good things again or avoid the bad things.”

Childress, a clinical associate professor of psychology in psychiatry, has been using neuroimaging techniques in an effort to map out the neuroanatomy of desire. Her work began years ago as she tried to understand craving, a cardinal

of the things they kept mentioning was that they all were seeing drug-abuse problems in their practices, and they didn’t learn enough about it in medical school because the elective was too brief” or the students failed to grasp the contents. As a result of that retreat, a full required course on substance abuse and addiction was squeezed into the curriculum.

Getting the course into the curriculum has not completely broken down the resistance among medical professionals to accepting addiction as a chronic disease. Kyle Kampman, M.D., reports that he is occasionally surprised, when giving a lecture on addiction, to hear the responses of some medical students – “that addiction isn’t really a disease.” That attitude, he says, is “part of the struggle.”

Yet according to O’Brien, the course on substance abuse has been effective in changing attitudes among many medical students. The problem, he notes, is

that when the students go to the wards, they are influenced by their senior residents and the attending physicians, many of whom presumably have not taken the addiction course in medical school.

“I remember one medical student who came back to me after taking the course,” says O’Brien. “He was doing this medicine rotation and he said, ‘Dr. O’Brien, I had this patient who is an alcoholic with really severe liver disease and esophageal varices, and he was coughing up blood and everything. And so we treated all these problems, and I asked the chief resident if I could refer this patient to the alcohol treatment program. And [the resident] said, ‘I don’t believe in that.’ So, essentially, what could the student do? This is like saying, ‘I’m going to give people with pneumonia an aspirin to keep their fever down, but I’m not going to treat the bacteria that’s causing the pneumonia.’”

– Lisa J. Bain

feature of addiction and one of the primary reasons for relapse. "One of the things we often heard from patients was that encountering things that were strongly reminiscent of their drug abuse – whether it was the sight of someone they had used drugs with, or the location where they had purchased it, or paraphernalia lying in the gutter, or even internal states that had sometimes preceded use of the drug – many of those things could set off a state of arousal and drug desire." That experience, she adds, often preceded a relapse.

Originally, Childress heard these stories from patients addicted to opiates, but later she heard similar stories from those addicted to cocaine. "They could often taste a little bit of cocaine back in their throat even though it was nowhere around, smell it even though it was not in the room. Their ears would be buzzing, head light, heart pounding. They'd feel a little whiff of euphoria. And of course, importantly, they would feel a very strong pull toward the drug." As she puts it, it is "the simplest kind of association learning."

Childress and a multidisciplinary group of investigators at Penn induced craving in detoxified cocaine users by showing them a video that simulates drug-taking behavior or shows paraphernalia or settings associated with drug taking. Next they used a brain-imaging technique called positron emission tomography (PET) to visualize activity in the subjects' brains. PET uses a radioactively labeled compound to detect regional changes in blood flow. The results of Childress's study, published in *The American Journal of Psychiatry* in 1999, made headlines across the country. "What we saw, and what we had predicted, was basically that old brain regions are involved not only in the experience of pleasure but in the anticipation and learning about it," says Childress. Previous research with animal models had shown that these regions of the brain play these roles. "But it had never been demonstrated until we began this work in humans that in



With positron emission tomography, Anna Rose Childress, Ph.D., has shown which regions of the brain experience craving.

anticipation of drugs, these structures could be differentially activated." Among cocaine users, the limbic regions of the brain, particularly the amygdala and anterior cingulate, showed an increase in activity, while another brain region called the basal ganglia showed a decrease in activity. This latter observation may help provide a neurological explanation for another phenomenon of drug addiction – that users seem to ignore or forget the negative consequences of their drug taking while they compulsively seek to satisfy their craving.

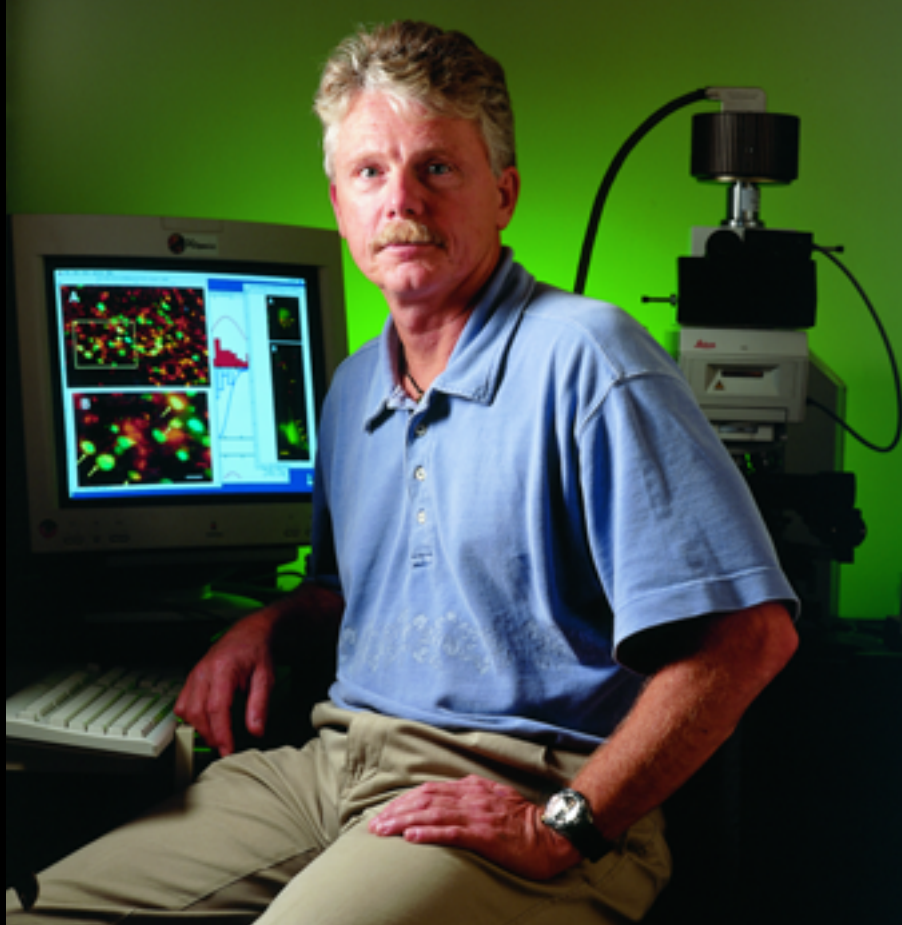
#### Next steps

Mapping the anatomical basis of craving, Childress asserts, is only the first step. "Basically all of these brain regions perform multiple functions and have multiple chemical messengers that are involved at each site. So the next level of question becomes not just where the action is in the brain – which areas light up or are working harder – but what's the neurochemistry?" Childress and col-

leagues have recently begun searching for the answer, again using PET scanning.

Neurons communicate with one another via neurotransmitters such as dopamine. When a neuron is stimulated, it releases chemicals called neurotransmitters, which cross the gap (called the synapse) between two neurons. The second neuron has receptors on its surface that bind the neurotransmitter. The binding of neurotransmitter to receptor may either activate or inhibit the post-synaptic neuron, depending on the specific receptor subtype and the neurotransmitter involved. Many neurotransmitters are involved in the brain's reward pathway as well as in brain circuits that process emotions, learning, and memory. Different drugs affect these neurotransmitter pathways in different ways.

Much of the attention in the addiction research community has focused on dopamine. Animal data suggest that when an animal is staring at a sex partner across a screen, or at a preferred food (rats, Childress notes, are particularly



Adrienne Geary

Gary Aston-Jones, Ph.D., has studied the experience of withdrawal in addicted rats.

fond of Cocoa Puffs), or at the signal for cocaine, dopamine is released in what Childress describes as “little gushes.” Her plan is to use tracers in the brain that have an affinity for dopamine receptors. As before, she will show subjects the video with cocaine associations before doing a PET scan. If the subject’s brain releases dopamine while viewing the video, the dopamine will compete with the tracer for the receptors. The image will thus be a mirror image; if more tracer is imaged, it means there was less dopamine competing for the receptor.

Another way to ask the neurochemical question, says Childress, is to pretreat patients with a medication that modulates brain dopamine and then observe whether this pretreatment blunts cue-induced craving and the activation of the critical brain areas. Such medications may act either directly or indirectly on brain dopamine. For example, Childress has been interested in using this approach to investigate whether a muscle relaxant called baclofen

might be effective in blunting craving. Baclofen works on the brain’s GABA (gamma-aminobutyric acid) system. GABA is one of the most prevalent neurotransmitters in the brain. Animal studies have shown that medications of this type affect many cocaine-related behaviors: for example, they reduce the animals’ enthusiasm for taking cocaine and block their preference for a location in which they previously received cocaine.

Childress had begun studies to assess the effectiveness of using baclofen to treat addiction in humans when a colleague at Presbyterian Medical Center called to say he had a patient that Childress would be interested in meeting. The patient was a paraplegic who had been taking baclofen for his spasms and who was also a cocaine user. To keep his spasms under control, he doubled his dose of baclofen. According to Childress, “He noticed when he took that dose, it seemed like the cocaine on the street was really not as good as it was before. He began eliminating doses and noticed that

the spasms returned, along with both the cocaine craving and the high he got from taking cocaine. In effect, the patient had done his own baclofen experiment, with dose response, titration of dose, omission of dose – as Childress puts it, “all the things that if I had a long time to do I would like to do.”

The patient’s experience provided more than information about the effectiveness of baclofen. The medication was clearly helpful to this patient in bringing his craving into a manageable range. “He did not feel literally pulled out of his wheelchair to go look for cocaine, as he did when he omitted baclofen or before he was on it.” Before the patient decided to stop using drugs – which he did decide during his stay at Presbyterian – he was still “planning his life around essentially a couple of hours of cocaine pleasure at the end of the month. So he wasn’t driven by craving, but made a conscious intellectual plan to forego his baclofen knowing he could have a few hours of pleasure.” The lesson, asserts Childress, is that reducing the craving for drugs alone is not likely to be enough for most people with an addiction. Even if a drug reduces cocaine craving quite a lot, it usually will not perform what Childress calls “a selective memoryectomy,” so that the person no longer even remembers cocaine or the high it brought. “The person will still be in the role of making an active decision of whether or not to continue.”

Investigators are also looking at other neurotransmitters that may play a role in addiction. “I doubt very much that in something as robust as addiction that one neurotransmitter and one system is the whole story,” says Gary Aston-Jones, Ph.D., professor of psychology in psychiatry and of pharmacology. In recent years, several studies, including those conducted by Aston-Jones and colleagues, have focused on the role of serotonin, a neurotransmitter that interacts with many neurotransmitter systems, including

dopamine. Through animal studies, the investigators have shown that administering the opiate morphine leads to an increase in serotonin transmission in the nucleus accumbens; furthermore, when morphine is withdrawn, the serotonin levels fall. Low serotonin levels have been linked with depression and compulsive behaviors. Clinical reports have suggested that drugs that inhibit the reuptake of serotonin, thus increasing the availability of the neurotransmitter, may decrease drug craving. These drugs, known as selective serotonin reuptake inhibitors or SSRIs, include Prozac (fluoxetine) and Zoloft (sertraline), drugs that are widely used to treat depression in humans. Aston-Jones has been using an animal model of cocaine and opiate dependence to try to understand the physiologic mechanisms whereby SSRIs might affect craving.

He focused on the experience of withdrawal. Rats that have been chronically treated with opiates experience physical symptoms of withdrawal such as anxiety, depression, and drug craving when the drugs are withheld. Aston-Jones compared a group of chronically morphine-treated rats (dependent) with a second group of rats that were given opiates acutely rather than chronically (non-dependent). When the drugs were withdrawn, both groups of rats expressed a preference for the environment where they received the opiate, although the dependent group showed a stronger preference. When the researchers treated the chronically treated rats with SSRIs, however, they found that two crucial indicators of withdrawal were alleviated: anxiety and the conditioned preference for the environment where they received the drug. In contrast, the acutely treated rats gained no benefit from the SSRI treatment. Aston-Jones was also able to show that even without subsequent administration of morphine, the chronically treated rats show decreased levels of serotonin transmission relative to acutely treated rats.

According to Aston-Jones, this study indicates that something in the brain of the chronically treated rats has changed and that the SSRIs may be rectifying a deficit induced by chronic exposure to opiates. He recently completed a second set of similar experiments using cocaine rather than opiates and had similar results. "I'm quite encouraged," he says, "because it suggests we might be looking at some common denominator."

### Probing at the molecular level

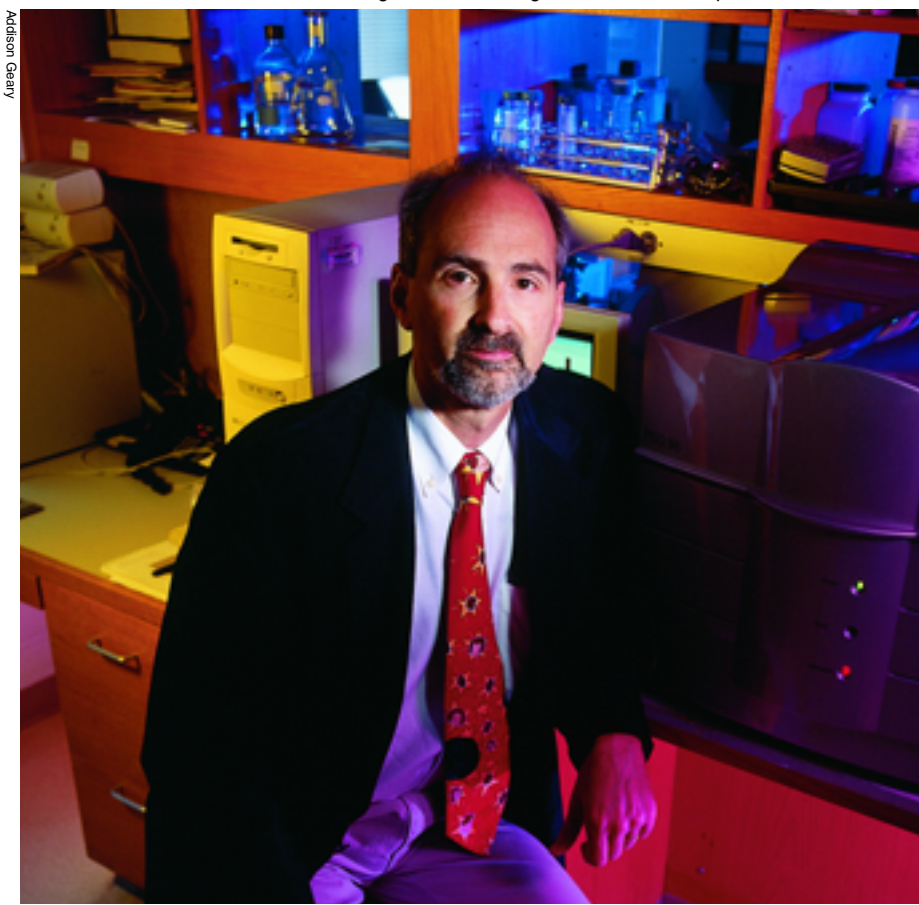
Questions remain in the effort to understand drug addiction and develop effective treatments. Why does one person become addicted and another does not? How is the brain of a person addicted to drugs different from the brain of someone who is not? The answers lie in understanding the changes in the brain at a molecular and cellular level and in learning how genetic differences influence an individual's tendency to travel the road from drug use to drug addiction.

Studies of families and twins suggest that 40-60 percent of the risk of becoming addicted is attrib-

utable to genetics. According to Wade H. Berrettini, M.D., Ph.D., professor of psychiatry and of genetics, a first-degree relative of a person dependent on heroin faces a tenfold increased risk of becoming addicted himself or herself. Explaining this observation in genetic terms is likely to be quite challenging. As with other complex diseases, multiple genes are likely to interact with environmental factors as well as with psychological and social factors. Nonetheless, the human genome is already revealing clues about drug addiction. In fact, Charles O'Brien predicts that the genome project will affect psychiatry more than any other area of medicine.

Scientists interested in addiction are using a variety of approaches to uncover secrets locked in the genome. One approach is to give drugs to animals and then look for changes in gene expression in certain areas of the brain. According to one literature review published this year, the expression of more than 100 genes is altered after exposure to various drugs of abuse. These genes are associated with a wide array of cellular func-

Wade Berrettini, M.D., Ph.D., has investigated the role of genetics in heroin dependence.



tions, such as up- or down-regulation of receptors and production of enzymes and other neurochemicals. Another approach is to select candidate genes that seem likely to be involved, and then look for sequence differences among different individuals.

Berrettini has been investigating the role of genetics for a variety of psychiatric disorders, including heroin dependence. He has focused on the idea that sequence variations in a gene that codes for an opioid receptor might help explain differential susceptibility to becoming addicted. "We started our interest in this gene because we had done genetic studies in the mouse that had pointed to the mu opioid receptor as being important," he says. "Sequence variation in this gene seemed to explain a fair amount of the variance in how much morphine a mouse would self-administer." Since then, he has moved into human studies of the gene for this particular receptor, examining sequence variations in certain regions of the gene. Other genes are also likely to be scrutinized in a similar manner – for instance, genes for other receptors

and transporter genes for neurotransmitters that are involved in drug addiction.

### **The payoff: better treatments**

The effort to understand the neurobiology of addiction has led to more effective treatments in several areas, although there is still much more to be done. According to Kyle M. Kampman, M.D., assistant professor of psychiatry, naltrexone is the best example of this progress. While most drugs used in psychiatry were discovered serendipitously, naltrexone is one of the few drugs that was developed as the result of a scientific theory about the neurochemistry of addiction. Naltrexone was originally developed to treat addiction to heroin. Interestingly, however, although naltrexone blocks the craving for alcohol, it does not block the craving for opiates. And as Kampman bluntly puts it, "If you find a medicine that doesn't do much for craving, it tends not to work too well." A second drug to treat alcoholism, acamprosate, is also available outside of the United States.

For heroin addiction, two drugs

– methadone and LAAM (l-alpha-acetyl-methadol) – are available and a third one (buprenorphine) is nearing approval by the Food and Drug Administration. All of these work by replacing opiates, but unlike heroin these agents are long acting. This property, said Charles O'Brien, allows people to live a normal life even if they are unable to eliminate the opiate completely. "When you take a long-acting opiate, such as methadone, it kinds of goes up and stays sort of steady," he explains. "There are some people who seem to have a built-in need to be on something, some kind of external opiate. They function very well on the opiate, but if you take it away they do poorly."

Unfortunately, as Kampman notes, there are no drugs available yet to treat cocaine addiction, although several, including baclofen, are under investigation. "One of the reasons, in my opinion, is that we've asked the medications to do too much. In the past we've basically tried to find a medication that could do everything for everybody." By trying to treat everyone with cocaine addiction in the same fashion, Kampman believes, researchers have overlooked the effectiveness of various drugs for certain subgroups of people.

Cocaine withdrawal, which can result in anxiety, sleep difficulties, appetite problems, irritability and depression, is usually less physically dramatic than withdrawal from heroin or alcohol, which can involve shaking, sweating, and seizures. Still, Kampman has found that people with significant cocaine-withdrawal symptoms tend to drop out more easily and not get clean. "We looked at that and came to the conclusion that these people are really different."

Kampman has been studying the effectiveness of two drugs commonly used for other conditions that appear to lessen withdrawal symptoms: propranolol, which is used to treat high blood pressure, and amantidine, a drug used to treat Parkinson's disease. Early studies produced mixed results; at times the drugs seemed

Kyle M. Kampman, M.D., found that patients who took regular doses of propranolol reduced their use of cocaine.



Adelson Geary

effective in relieving withdrawal while at other times they appeared ineffective. "When you get results like that," says Kampman, "you start to think there's a subgroup embedded in there that it may be effective for."

For Kampman, the mechanisms of action of the two drugs suggested they might be useful for treating cocaine withdrawal. Amantidine stimulates the release of dopamine; propranolol blocks the effects of adrenaline. People who use cocaine get a strong adrenaline rush in response to cues that remind them of cocaine; they also are very sensitive to the effects of adrenaline during withdrawal. Kampman and his colleagues thought that propranolol might block some of the physical symptoms of craving. In addition, the drug has been shown to affect memory. Kampman refers to a study in *Science* showing that propranolol reduced emotional arousal and, as a result, the memory of events or things that were emotionally arousing. According to Kampman, O'Brien suggested that he try the drug with cocaine patients. "Dr. O'Brien sees this and says, 'well, what is cocaine craving but an emotionally arousing memory of prior cocaine use? So let's see if we can have that effect on cocaine.'"

The results of their eight-week study indicated that those patients with severe withdrawal symptoms stayed in treatment longer and used less cocaine when they took regular doses of propranolol. An earlier study led by Kampman had shown that amantidine reduced craving in cocaine patients with significant withdrawal symptoms. The next step will be to see whether giving propranolol and amantidine together will yield better results than either drug alone, or than a placebo.

New drugs are in the pipeline, as well as familiar drugs for new uses. One class of drugs that has generated much interest for treatment of cocaine craving is the dopamine receptor partial agonists. "Partial agonists are

chameleon-like medications that change their activity depending on the level of the endogenous transmitter around them," explains Childress. These drugs address a dilemma in the effort to combat craving – that is, that cocaine craving can result from either too much or too little dopamine. In a chronic user of cocaine, halting the use of cocaine can lead to a dopamine-depleted state; yet exposure to cues can stimulate enhanced dopamine activity. In response to these varying states, partial agonists stimulate dopamine receptors when dopamine levels are low and block the receptors when dopamine levels are high. Says Childress, "It's really fascinating to think that we might have medications that could be able to essentially offer a moment-to-moment regulation of dopamine, depending on where the patient is."

#### Resistance to change

Despite increasing medical and scientific evidence that demonstrates the biological basis of addiction and the necessity of long-term treatment, much of the general public and many professionals involved in treatment continue to view addiction as a social problem rather than a health problem. Since the beginning of the 20<sup>th</sup> century, the tendency in the United States has been to criminalize addiction. "Most of the rest of the world thinks of it as a medical problem," said O'Brien. "The 'war on drugs' uses the metaphor of war and spends two-thirds of the money on interdiction, which means burning poppy fields and shooting down planes in Peru. We have many more people in our prisons than any other country in the world, and it's largely because of the drug war."

As a result, while research is well funded, there are too few treatment slots available for the people in need of treatment. Much of the treatment that is available is delivered outside the health care system in 12-step programs that often reject the use of drugs to

treat addiction. According to Volpicelli, these programs are often run by recovering addicts who kicked their habits without medical treatment; they often believe that other addicts can do so as well, as long as they have the motivation.

The view that addiction is a social rather than medical problem is further reflected in the medical community. Most medical school curricula offer little training in the treatment of addiction, although since the late 1980s, a course on drug addiction is required at Penn's medical school (see box on pp. 8-9). Furthermore, there is resistance among physicians to treat drug addiction as a chronic, rather than acute, illness. A. Thomas McLellan, Ph.D., an adjunct professor of psychiatry at the Treatment Research Center, is the lead author of a paper in *JAMA* (October 4, 2000) that lays out the case for regarding addiction as a chronic disease. McLellan compares addiction to three other common chronic diseases — diabetes, hypertension, and asthma. He demonstrates that these illnesses share several features, including similar heritability estimates, frequent problems with treatment compliance, and the influence of personal behaviors on progression of disease.

According to O'Brien, the *JAMA* paper precipitated some strong reactions. Physicians who wrote to the journal were indignant that addiction would be compared to these other diseases, which do not carry a comparable stigma. In O'Brien's view, "Doctors are just like all other citizens and tend to blame the addict. They say, 'They brought it on themselves; they voluntarily took this drug.'" In reality, he adds, "many, many people are exposed to drugs but not everybody gets hooked, so there's a lot that you're not responsible for. But once you get hooked, it's really an involuntary process." ■

*Lisa Bain last wrote for Penn Medicine about Dr. Katherine High's gene therapy for dogs with hemophilia (Fall-Winter 2000).*



Although very much a man of his own time, a Penn Med alumnus has fashioned a second career outside medicine, inspired by the 18<sup>th</sup> century's most celebrated portrait sculptor.



## In the Style of H O U D O N

*By John Shea*

John Lanzalotti's marble bust of James Wilson, founder of Penn's Law School.

Jean-Antoine Houdon (1741-1828) seemed magically adept at neoclassical sculpture, with its traditional themes and idealized beauty. Yet he could also bring naturalistic touches to his busts of famous people, evoking their individuality. Today, he is known for his statues and busts of people like Voltaire, Catherine the Great, and Benjamin Franklin. Indeed, John A. Lanzalotti, M.D. '75, asserts that Houdon's bust of Franklin "has become a part of the iconography of the United States." As Lanzalotti puts it, "all our concepts of the Founding Fathers come from Houdon."

One of the young nation's leading citizens whom Houdon did not sculpt was James Wilson. Wilson signed the Declaration of Independence, served as a delegate to the Constitutional Convention, and was appointed one of the first Justices of the United States Supreme Court. The first lecturer in law at any American institution of higher education, Wilson is recognized as the founder of Penn's Law School.

To commemorate Wilson's legacy, the Law School's Class of 2001 looked around for someone to create a marble bust of the School's founder. Houdon, unfortunately, was nearly two centuries dead. But the representatives of the graduating class found someone to step in, chisel in hand: Lanzalotti, who has developed a commercially successful business creating busts of historical figures. During this May's Alumni Weekend, Lanzalotti's bust of Wilson was unveiled and presented to the school.

How did Lanzalotti, who had been practicing as a plastic surgeon, general surgeon, and generalist physician, come to be one of Houdon's heirs? The short answer is managed care, but the story is somewhat more complicated than that. At any rate, the immediate impetus was his admiration for four Houdon busts of the Founding Fathers that Jefferson kept in his "gallery of worthies" at Monticello. During a visit, Lanzalotti became interested in buying copies of Houdon's work but was told there weren't any to sell. Undaunted, Lanzalotti decided to try making his own copies. He was so



successful that today Lanzalotti's copies of the four Houdon sculptures are on sale in the gift shop at Colonial Williamsburg.

"I'm totally self-taught," he says. He consulted texts on the art and the materials, then set to work, apparently marshalling the same determination that helped him get through Penn's medical school in three years. (He came to Penn after serving as an engineering officer in the Navy, already possessing what a friend calls "a rich life experience.") Lanzalotti turned to portrait sculpture in earnest in 1996 – and he believes he's getting better. "I'm amazed at some of the stuff I turn out," he says. No false modesty here. Indeed, a brief visit to his website ([www.williamsburgsculpture.com](http://www.williamsburgsculpture.com)) reveals an impressive range of art, from what he calls the Houdon Reproduction Collection to recreations of Egyptian sculpture to copies of historic paintings that have medical or scientific themes to detailed medical illustrations (for example, one shows the path of the facial nerve that innervates the muscles of facial expression).

Henry R. Bleier, M.D., G.M.E. '77, M.B.A., a clinical professor of psychiatry at Penn who is based at the Veterans Affairs Medical Center, met Lanzalotti nearly 30 years ago when Lanzalotti was doing a clerkship in medicine and Bleier was his supervising intern. He calls Lanzalotti a "polymath" who "excelled at virtually everything he did." According to Bleier, the average person might be able to pick up an instruction manual and build a model of some sort; in contrast, Lanzalotti "produces an item of artistic excellence."

Although Williamsburg Sculpture is a relatively new venture, Lanzalotti had shown artistic inclinations as far back as high school. The summer before he took gross anatomy at Penn, he points out, he was doing anatomical illustrations. Not surprisingly, his career as a plastic surgeon also fostered his artistic talents. More recently, hand

in hand with his work as a medical-legal consultant, he has made detailed medical illustrations. As he puts it, "I've got a whole library of body parts."

Still, creating sculptures was a new challenge. "It's like a surgical operation," he says. "I'm very efficient." Doing the clay models usually requires from six to eight hours. Lanzalotti emphasizes that there is a technical component and an artistic component. He also notes that, much as in the days of Michelangelo, the process of making a sculpture begins with a stonecutter knocking out some stone for the artist. From that point, Lanzalotti may spend anywhere from two to five weeks "working every day and all day long." A large part of that time is devoted to capturing the facial expressions and "projecting a certain personality" as well as smoothing the texture of the stone.

Stanley Taub, M.D., is in the rare position of being able to evaluate and appreciate Lanzalotti's work both as a plastic surgeon and a sculptor – he, too, is both. "He does nice work as a sculptor," says Taub, who adds that Lanzalotti's embrace of the neoclassical style "is a natural for him." Like plastic surgery, asserts Taub, sculpture "is all in the hands – the hands are in touch with a part of the brain." Both activities "have a sense of purpose and design, there's no guesswork." Yet at the same time, Taub recognizes "a very Zen-like feeling" to plastic surgery and sculpture. He believes that visualization – seeing with "the mind's eye" – is very important in both.

For all his talents, it is doubtful that Lanzalotti would be following in Houdon's path if his circumstances as a plastic surgeon and general physician had not changed. After taking his residency in plastic surgery, Lanzalotti settled in Williamsburg in 1982. He also enjoyed doing generalist medicine and felt he had success as a diagnostician. "I picked



Top: Lanzalotti's copy of the Colonial Williamsburg unicorn (marble, 1999).  
Bottom: A commissioned portrait bust of Jacqueline Kennedy Onassis.



up a lot of early cancer patients," he says, directing them to subspecialists for confirmation and treatment. On the whole, the 1980s were a lucrative time for his practice. Then came the era of managed care: "It's been devastating." For one thing, he says, all the other independent medical practices in the region were bought out. Lanzalotti lost his primary-care patients because he had not taken his residency in a comparable field and the managed-care organizations would no longer refer patients to his practice.

Given his strong feelings on the matter, it is not surprising that Lanzalotti has published about health-care reform – for example, in the *Journal of the Medical Association of Georgia*. The essence of his views is that "medicine is like a sacred trust." "You're doing what's in the best interests of the patient," he says, or you shouldn't be doing it at all. Bleier points out that Lanzalotti serves as a consultant to the state legislature of Virginia on health matters.

Besides sculpture, Lanzalotti has found other ways to compensate for a reduced medical practice. He has been an adjunct faculty member at the College of William and Mary. There he teaches some of the medical humanities. He especially enjoys dealing with the students, pointing out that some of them even have asked him to hood them at their graduation ceremonies. Another interest of his that burgeoned since the rise of managed care is consulting in medical-legal matters. In fact, he says that one law firm has asked him to go to law school. "I'm toying with that idea right now," he says. This range of passions and accomplishments has led both Bleier and Taub to describe Lanzalotti as someone who approaches "the Renaissance man."

**I**t's clear that Lanzalotti takes his sculpture very seriously, both as practitioner and as student of the art. On his website, he

describes Houdon's portrait of Franklin, which Lanzalotti copied in marble three years ago. Instead of an idealized portrait, there are touches of naturalism, artistic choices that show how Houdon went about evoking a complicated sense of character: "The expression on Franklin's face seems to suggest his benevolence, wisdom, humor, and his forthright qualities. . . . His hair, thin on top, flows down over his ears and shoulders. Houdon emphasized the wrinkles at the corners of his eye, giving his appearance from certain angles a look of weariness and even apprehension."

Lanzalotti brings the same close attention and awareness of context when he speaks about one of his own works in progress, a statue of Justice commissioned for the Williamsburg-James City County Courthouse. Eschewing naturalistic touches, Lanzalotti says he was striving for a neoclassical ideal. Unlike the solid, somewhat masculine Statue of Liberty, Lanzalotti's embodiment of Justice is "light, very graceful, very flowing." The statue, more than six feet high, will be carved in white marble. Justice holds a sword in her right hand and scales in her left; both iconic accouterments are cast in bronze with a gold patina. The lightness of the female figure contrasts with the heaviness of sword and scales – an attempt, says Lanzalotti, "to counterbalance the gravity of the legal system."

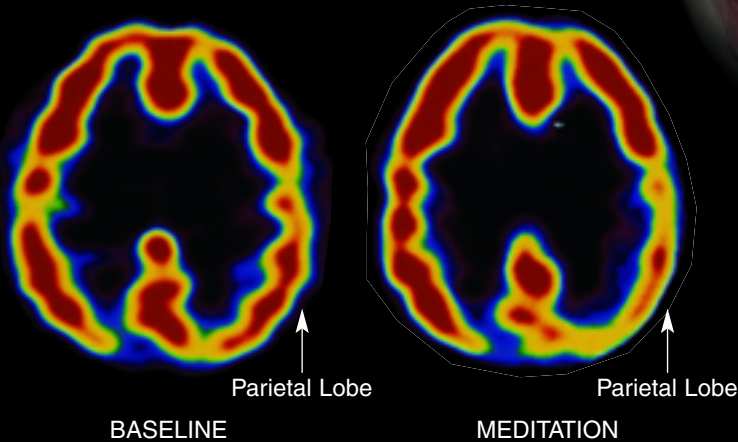
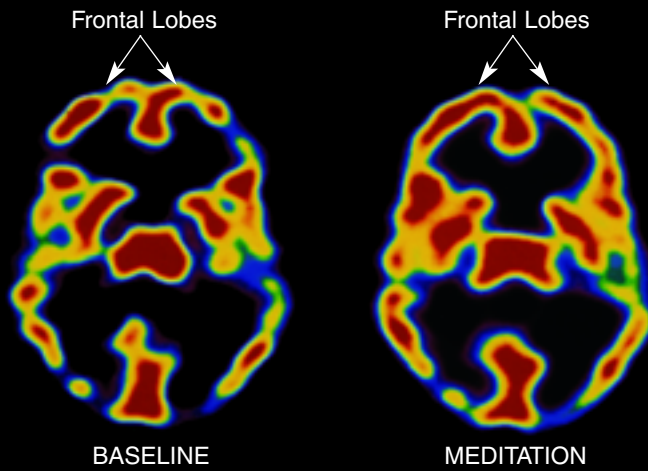
Although Lanzalotti can choose among several career paths, sculpture seems paramount at the moment. "Sculpture frees him," says Taub. That may be. What's undeniable is that Lanzalotti grew more animated when talking about the many other historical figures associated with the University of Pennsylvania that could well deserve commemorative busts of their own. ■



*Top:* Lanzalotti's model for Justice, commissioned for the Williamsburg – James City County Courthouse.  
*Bottom:* Lanzalotti's painted plaster bust of Nefertiti.



# A PHOTOGRAPH OF GOD?



**Two Penn alumni explore the human biology of belief, bringing with them the latest scientific tools.** For several years, Andrew B. Newberg, M.D. '93, has been fascinated by spiritual experience and by the possibility of studying it through the high-tech techniques of modern medicine. In 1991, while still in medical school, he began a fruitful collaboration with Eugene D'Aquili, M.D. '66, Ph.D., a psychiatrist who also had a master's degree in anthropology. Eventually, they began to study the brains of meditating practitioners of Buddhism and of Roman Catholic nuns at prayer. To do so, they used one of the tools of Newberg's radiologic trade, a SPECT camera, which measures

brain activity. Their finding is that the human brain alters during intense contemplation – and that these changes can be objectively observed and recorded. Newberg and D'Aquili published their research in *The Mystical Mind: Probing the Biology of Religious Experience* (1999). Earlier this year, Ballantine Books issued Newberg and D'Aquili's *Why God Won't Go Away: Brain Science and the Biology of Belief*, written with Vince Rause. The new book presents their findings for a more general reading public. D'Aquili died in August, 1998. Newberg is now assistant professor of radiology at Penn. What follows is an excerpt from the first chapter. (The "large university hospital" cited in the text is HUP.)

In a small, dark room at the lab of a large university hospital, a young man named Robert lights candles and a stick of jasmine incense; he then settles to the floor and folds his legs easily into the lotus position. A devout Buddhist and accomplished practitioner of Tibetan meditation, Robert is about to begin another meditative voyage inward. As always, his goal is to quiet the constant chatter of the conscious mind and lose himself in the deeper, simpler reality within. It's a journey he's made a thousand times before, but this time, as he drifts off into that inner spiritual reality – as the material world around him recedes like a fading dream – he remains tethered to the physical here and now by a length of common cotton twine.

One end of that twine lies in a loose coil at Robert's side. The other end runs beneath a closed laboratory door and into an adjoining room, where I sit, beside my friend and longtime research partner Dr. Eugene d'Aquili, with the twine wrapped around my finger. Gene and I are waiting for Robert to tug on the twine, which will be our signal that his meditative state is approaching its transcendent peak. It is this peak moment of spiritual intensity that interests us.

For years, Gene and I have been studying the relationship between religious experience and brain function, and we hope that by monitoring Robert's brain activity at the most intense and mystical moments of his meditation, we might shed some light on the mysterious connection between human consciousness and the persistent and peculiarly human longing to connect with something larger than ourselves.

Whatever Robert calls this deeper consciousness, he claims that when it emerges during those moments of meditation when he is most completely absorbed in looking inward, he suddenly understands that his inner self is not an isolated entity, but that he is inexplicably connected to all of creation. To the traditional scientific mind, of course, this description is useless. Years of research, however,

have led Gene and me to believe that experiences like Robert's are real, and can be measured and verified by solid science. That's exactly why I'm huddling, beside Gene, in this cramped examination room, holding kite string between my fingers: I'm waiting for Robert's moment of mystical transcendence to arrive, because I intend to take its picture.

We wait one hour, while Robert meditates. Then I feel a gentle jerk on the twine. This is my cue to inject a radioactive material into a long intravenous line that also runs into Robert's room, and into a vein in his left arm. We wait a few moments more for Robert to end his meditation, then we whisk him off to a room in the hospital's Nuclear Medicine Department, where a massive, state-of-the-art SPECT camera awaits. In moments, Robert is reclining on a metal table, the camera's three large crystal heads orbiting his skull with a precise, robotic whir.

The SPECT camera (the acronym stands for single photon emission computed tomography) is a high-tech imaging tool that detects radioactive emissions. The SPECT camera scans inside Robert's head by detecting the location of the radioactive tracer we injected when Robert tugged on the string. Because the tracer is carried by blood flow, and because this particular tracer locks almost immediately into brain cells and remains there for hours, the SPECT scans of Robert's head will give us an accurate freeze-frame of blood flow patterns in Robert's brain just moments after injection – at the high point of his meditative climax.

Increased blood flow to a given part of the brain correlates with heightened activity in that particular area, and vice versa. Since we have a good idea of the specific functions that are performed by various brain regions, we expect the SPECT images to tell us a lot about what Robert's brain was doing during the peak moments of his meditation.

We aren't disappointed. The finished scan images show unusual activity in a small lump of gray matter nestled in the top rear sec-

tion of the brain. The proper name for this highly specialized bundle of neurons is the posterior superior parietal lobe, but Gene and I have dubbed it the orientation association area, or OAA.

The primary job of the OAA is to orient the individual in physical space – it keeps track of which end is up, helps us judge angles and distances, and allows us to negotiate safely the dangerous physical landscape around us. To perform this crucial function, it must first generate a clear, consistent cognition of the physical limits of the self. In simple terms, it must draw a sharp distinction between the individual and everything else, to sort out the you from the infinite not-you that makes up the rest of the universe.

To do its job so well, the orientation area depends on a constant stream of nerve impulses from each of the body's senses. The OAA sorts and processes these impulses virtually instantaneously during every moment of our lives. It manages a staggering workload at capacities and speeds that would stress the circuits of a dozen super computers.

So, not surprisingly, the baseline SPECT scans of Robert's brain taken before his meditation, while he was in a normal state of mind, show many areas of Robert's brain, including the orientation area, to be centers of furious neurological activity. This activity appears on the scans in vibrant bursts of brilliant reds and yellows. The scans taken at the peak of Robert's meditative state, however, show the orientation area to be bathed in dark blotches of cool greens and blues – colors that indicate a sharp reduction in activity levels.

This finding intrigued us. We know that the orientation area never rests, so what could account for this unusual drop in activity levels in this small section of the brain?

As we pondered the question, a fascinating possibility emerged: What if the orientation area was working as hard as ever, but the incoming flow of sensory information had somehow been blocked? That would explain the drop in

brain activity in the region. More compellingly, it would also mean that the OAA had been temporarily “blinded,” deprived of the information it needed to do its job properly.

What would happen if the OAA had no information upon which to work? we wondered. Would it continue to search for the limits of the self? With no information flowing in from the senses, the OAA wouldn’t be able to find any boundaries. What would the brain make of that? Would the orientation area interpret its failure to find the borderline between the self and the outside world to mean that such a distinction doesn’t exist? In that case, the brain would have no choice but to perceive that the self is endless and intimately interwoven with everyone and everything the mind senses. And this perception would feel utterly and unquestionably real.

This is exactly how Robert and generations of Eastern mystics before him have described their peak meditative, spiritual, and mystical moments. Robert was one of eight Tibetan meditators who participated in our imaging study. Each was subjected to the same routine, and in virtually every case, the SPECT scans showed a similar slowing of activity in the orientation area, occurring during the peak moments of meditation.

Later, we broadened the experiment and used the same techniques to study several Franciscan nuns at prayer. Again, the SPECT scans revealed similar changes that occurred during the sisters’ most intensely religious moments. Unlike the Buddhists, however, the sisters tended to describe this moment as a tangible sense of the closeness of God and a mingling with Him.

As our study continued, and the data flowed in, Gene and I suspected that we’d uncovered solid evidence that the mystical experiences of our subjects – the altered states of mind they described as the absorption of the self into something larger – were not the result of emotional mistakes or simple wishful thinking, but were associated instead with a series of observable neurological events, which, while unusual, are not outside the range of nor-

mal brain function. In other words, mystical experience is biologically, observably, and scientifically real.

This result did not surprise us. In fact, it was exactly what all our previous research had predicted. For years, we had scoured the scientific literature for studies examining the relationship between religious practices and the brain, searching for insights into the biology of belief. Our approach had been broad and inclusive. We found some studies that examined simple physiology – for example, they measured changes in blood pressure of people as they meditated. Other studies aimed at loftier stuff such as measuring the healing powers of prayer. We read the research on near-death experiences, studied mystical states induced by epilepsy and schizophrenia, looked at the data on hallucinations triggered by drugs as well as electrical stimulation of the brain.

Besides our scientific readings, we also looked for descriptions of the mystical components of world religions and mythologies. Gene, in particular, researched the ritual practices of ancient cultures and looked for a relationship between the emergence of ritual behavior and the evolution of the human brain. An abundance of information exists that is relevant to the relationship between religious ritual and the brain, but little of it had been sorted or synthesized into a coherent framework.

Yet as Gene and I sifted through mountains of data on religious experience, ritual, and brain science, important pieces of the puzzle came together and meaningful patterns emerged. Gradually, we shaped a hypothesis that suggests that spiritual experience, at its very root, is intimately interwoven with human biology. That biology, in some way, compels the spiritual urge.

The SPECT scans allowed us to begin testing this hypothesis by observing the actual brain activity of people engaged in spiritual practices. The images do not prove our hypothesis beyond doubt but they strongly support it by showing that, in moments of spiritual behavior, the human brain appears

to behave as our theory predicts that it would. These encouraging results deepened our enthusiasm for our work, and sharpened our interest in the fascinating questions provoked by our years of research. Questions like: Are human beings biologically compelled to make myths? What is the neurological secret behind the power of ritual? Are the transcendent visions and insights of the great religious mystics based on mental or emotional delusions, or are they the result of coherent sensory perceptions shaped by the proper neurological functioning of sound, healthy minds? Could evolutionary factors such as sexuality and mating have influenced the biological development of religious ecstasy?

As we labored to better understand the implications of our theory, we found ourselves confronted again and again by one question that resonated more deeply than any other: Had we found the common biological root of all religious experiences? And if so, what did such an understanding say about the nature of the spiritual urge?

A skeptic might suggest that a biological origin to all spiritual longings and experiences, including the universal human yearning to connect with something divine, could be explained as a delusion caused by the chemical misfirings of a bundle of nerve cells.

But the SPECT scans suggested another possibility. The orientation area was working unusually but not improperly, and we believe that we were seeing colorful evidence on the SPECT’s computer screen of the brain’s capacity to make spiritual experience real. After years of scientific study, and careful consideration of our results, Gene and I further believe that we saw evidence of a neurological process that has evolved to allow us humans to transcend material existence and acknowledge and connect with a deeper, more spiritual part of ourselves perceived of as an absolute, universal reality that connects us to all that is. ■

*From Why God Won’t Go Away, by Andrew Newberg, M.D. Copyright (c) 2001 by Andrew Newberg, M.D. Reprinted by arrangement with Ballantine Books, a division of Random House, Inc.*

**T**he cover of the Class of 1951's Scope reveals some of the typical levity of such books: the drawing shows a diapered tot approaching a rather imposing set of doors, which could very well be leading into the John Morgan Building. The tot bears a satchel labeled "Frosh." To the right of the drawing, heading out – but presumably at a much slower pace – is a severely stooped old-timer with long white beard and cane. He grasps a rolled-up diploma: in short, the new graduate, shuffling off into the future.

Much of the rest of the yearbook, especially the photo captions and cartoons, carried on this tone. One notable exception is the message from the dean, John McK. Mitchell, M.D., which was sober and high-minded: "In this time of

*urgent need for trained workers in every field, the demand for your services as physicians is almost without parallel. . . . If the demand for your services is great, your obligation to the community is correspondingly increased. While no one will deny your right to consider your personal advantage, immediate expediency should never be permitted to cloud your view of the more distant horizons. . . . We have confidence that you will make your choices wisely and, having chosen, will acquit yourself well."*

Now, 50 years later, some of those distant horizons are indeed here, and the time seems right to take a look at some of the paths taken, the choices made, by the members of the Class of 1951 who answered their reunion questionnaires.

# Celebrating the Class of '51



**1 Leeon F. Aller, M.D.,** and his wife of 55 years, Virginia, reside in Snohomish, Wash. Emeritus professor of family practice at the University of Washington, he remains active in the medical mission work he began many years ago. In 1991, he and his wife founded the Hands for Peacemaking Foundation, a non-profit organization that "teaches and engages in actions and programs developing human services in Central America and throughout the world." A former president of the Washington Academy of Family Physicians, Dr. Aller was named America's Family Physician of the Year by the American Academy of Family Physicians in 1987. He has also been honored by the U.S. Military and the Boy Scouts of America. He and Virginia had three children, adopted seven more, and had 80 foster children.

**2 Irvin C. Arno, M.D.,** Boynton Beach, Fla., retired in 1986. A specialist in obstetrics and gynecology, he taught at Penn's Graduate School of Medicine and at the Temple University School of Medicine. He remembers Dr. Albert Kligman as the most dynamic lecturer during his years as a medical student. Dr. Arno enjoys fishing, golfing, traveling, and sculpting. He and his wife Maxine had three children and have six grandchildren.

**3 Eleanor M. Aurand, M.D.,** Lewiston, Pa., specialized in pediatrics until her retirement in 1987. She is a life member on the Salvation Army Advisory Board.

**4 Ross O. Bell Jr., M.D.,** lives in Wheeling, W.Va., with his wife of 52 years, Wileta. Together they have five children and 14 grandchildren. Dr. Bell served as chairman for the Department of Pathology at the Ohio Valley Medical Center in Wheeling until his retirement in 1990, specializing in anatomic and clinical pathology.

**5 F. D. Beyer, M.D.,** Greensburg, Pa., retired from pathology in 1998. He spends time playing golf and the stock market. A former assistant professor at the University of Pittsburgh, he received the Excellence in Education Award from Frick Hospital. He also serves as a laboratory inspector. He and his wife Pat have two sons.

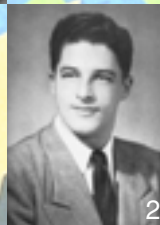
**6 Henry P. Brown III, M.D.,** Enfield, N.H., a retired physician, is described by his wife, Patricia, as "a genuine country doctor who delivered half the people in old Enfield." Formerly on the staff of the Alice Peck Day Hospital, he has also been chairman of the hospital's board. He has served on the planning committee of local schools, volunteered for Planned Parenthood, the Girl Scouts, and 4-H, and served as a director of the Grafton County Senior Citizens Council. The people of Le Raysville, Pa., named a new clinic after him.

**7 Laurence T. Browne, M.D.,** Philadelphia, writes that he plans to retire from internal medicine in the year 2010. He is currently a clinical associate professor of medicine at the Medical College of Pennsylvania, senior attending physician at Lankenau Hospital, and director of the Presidential Medical Center in Philadelphia. Dr. Browne is also the executive and founder of the Philadelphia Ad-Hoc Committee to Defend Health Care. In his free time, he enjoys photography, classical music, and studying the history of medicine. He has three children, all of whom work in the field of medicine.

**8 William Keegan Buchanan, M.D.,** lives in Hudson, Ohio, with his wife of 54 years, Celeste. They have one daughter and one granddaughter. Dr. Buchanan was a fellow of the American College of Anesthesiologists and served on the staff at St.



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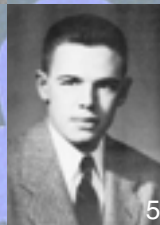
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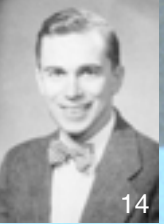
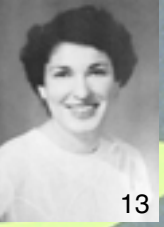
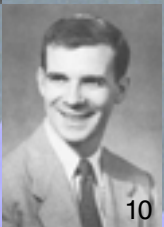
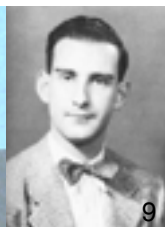


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Francis Hospital in Pittsburgh until his retirement in 1980. He is currently researching his family history and building his collection of American Indian and Civil War artifacts.

**9 J. Lincoln Cain, M.D.**, and his wife, Rosemary, live in Wakefield, R.I. Dr. Cain was chief of radiology at Waltham Hospital in Massachusetts for 34 years. Later, he worked as a radiologist at Rhode Island Hospital and as a clinical assistant professor at Brown University until retiring in 1995. He was a fellow of the American College of Radiology. Dr. Cain and his wife have five children and thirteen grandchildren.

**10 William R. Campbell, M.D.**, Salisbury, Md., retired as an orthopaedic surgeon in 1985. He now enjoys playing bridge, golfing, and boating. He and his wife Marilyn have four children.

**11 Theodore B. Cohen, M.D.**, still works full time in the field of adult and child psychiatry. In addition to teaching, he has been the chairman of the Vulnerable Child Subcommittee and Discussion Group of the American Psychoanalytical Association. He has published three volumes on the "vulnerable child" and has received the B'nai B'rith Award for services to children. He has one son and two grandchildren. In his spare time, Dr. Cohen plays tennis, gardens, and maintains a bird and animal sanctuary.

**12 Elizabeth B. Connell, M.D.**, lives in Atlanta with her husband, Howard Tatum, M.D., Ph.D. She retired in 1997 but continues to consult, write, and lecture on obstetrics and gynecology. Dr. Connell has taught at Emory University, Northwestern University, and Columbia University. She worked with Planned Parenthood and the United States Food and Drug Administration, including serving as workshop mod-

erator in 1994 on "Alternatives to Silicone Breast Implants." In 1993, she received the Vitality Award from the National Osteoporosis Foundation. She has six children and five grandchildren.

**13 Nancy Boucrot Cummings, M.D.**, has lived and worked in Washington, D.C., for the past 42 years. Currently she is senior biomedical advisor for the National Institute of Diabetes and Digestive and Kidney Diseases, clinical professor of medicine at Georgetown University School of Medicine, associate professor of community and family medicine at Howard University College of Medicine, and a fellow at the Kennedy Institute of Ethics. She is the recipient of numerous fellowships to study infantile paralysis, nephrology, and, more recently, bioethics. In her free time, Dr. Cummings enjoys attending the opera, ballet, and symphony; she also sits on the Circles Board of the Kennedy Center for Performing Arts. Her three children and seven grandchildren live on three different continents.

**14 Drs. Ruth Abrams and E. Archer Dillard Jr.** met in medical school and will celebrate their 50th wedding anniversary on June 13. Both retired in 1990 after many years teaching at the University of Texas Medical Branch in Galveston. Dr. Abrams specialized in pediatrics and Dr. Dillard in obstetrics and gynecology. They now live in College Station, Texas, and Boone, N.C. Dr. Dillard sits on the board of directors at Hebron County Ministries, a Christian home for alcoholics and drug addicts, while Dr. Abrams spends time gardening at Hebron and singing in the church choir. They look forward to continuing their charity work and have traveled to Belize five times on medical missions. They have three children and six grandchildren.

**15 Victor H. Frankel, M.D.,** New York City, retired from orthopaedic surgery in 2000. He is president emeritus of the Hospital for Joint Diseases in New York, professor of orthopaedic surgery at New York University School of Medicine, and a docent in orthopaedic surgery for the University of Uppsala in Sweden. Dr. Frankel has received various awards for his research in biomechanics, including the United States Ski Association Award of Merit for Research. He was made a Knight Commander of the Royal Order of the Polar Star by King Carl Gustaf XVI of Sweden, in recognition of his promotion of Swedish-American research programs and educational studies.

**16 William F. Gebhart, M.D.,** recently moved to Scottsdale, Ariz., after practicing internal medicine and nephrology in Santa Barbara, Calif., for 42 years. During that time he also served on the board of directors of the Southern California Medical Council and as co-medical director of the Santa Barbara Community Dialysis Center. Dr. Gebhart and his wife Rosemarie have been married nine years.

**17 James W. Grifone, M.D.,** lives in Seal Beach, Calif., with his wife of 43 years, Louise. He retired from internal medicine in 1992 but remains very active in Lions Club International and still serves as medical advisor for a Diabetes Awareness Program. He recalls that shortly after graduation, he and classmate Ross Bell found themselves working together in the Far East, serving as medical officers in the United States Army Medical Corps.

**18 William H. Harris, M.D.,** Belmont, Mass., is the Alan Gerry Clinical Professor of Orthopaedic Surgery at Harvard Medical School and chief of adult reconstructive surgery at Massachusetts General Hospital. He is a ten-time recipient

of the Award for Outstanding Research in Hip Surgery from The Hip Society and a two-time recipient of the Kappa Delta Award for Outstanding Research in Orthopaedic Surgery. Dr. Harris has also been honored with the Maurice Muller Award for Lifetime Achievement in Orthopaedic Surgery. He and his wife Nan have four children and five grandchildren.

**19 Walter L. Henley, M.D.,** lives in New York City with his wife Edith. They have two daughters. Dr. Henley retired in 1998 after teaching pediatrics for over forty years and ophthalmology for over twenty years at Mount Sinai School of Medicine in the City University of New York and the Albert Einstein College of Medicine of Yeshiva University. He also worked in pediatrics at Mount Sinai Hospital, Beth Israel Medical Center, and the Hospital for Joint Diseases.

**20 John E. Keith, M.D.,** retired from orthopaedic surgery in 1992. A former associate professor at the Medical College of South Carolina, he served as president of the South Carolina Orthopaedic Association. Dr. Keith has also been a fellow of the American College of Surgeons. He now lives in Spartanburg, S.C., with his wife Kitty; they have four children and eleven grandchildren. He hopes to organize a free dental clinic in Spartanburg to aid the working poor. He spends his free time golfing and fishing.

**21 Harry H. Kretzler, M.D.,** and his wife Jean live in Seattle. Retired from orthopaedic surgery last year, he taught orthopaedics at the University of Washington School of Medicine and served as orthopaedic consultant to the Rainier State School for more than twenty years. Dr. Kretzler has also been the team physician for a number of sports clubs, including the United States

World Cup Ski Team and the United States Olympic Team, and has served on physician panels for the National Football League as well.

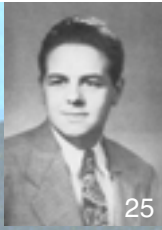
**22 John B. Kucharczuk, M.D.,** Allentown, Pa., still practices obstetrics and gynecology. He and his wife of 40 years, Helen, have two children and three grandchildren. In his leisure time, Dr. Kucharczuk enjoys photography and working with computers, watches, and clocks.

**23 Jerome M. Levine, M.D.,** and his wife Bernice, New Rochelle, N.Y., have been married for 53 years and have three children. Dr. Levine continues to practice psychiatry and psychoanalysis in New York City; he also teaches at the New York University School of Medicine. In his free time he enjoys music, languages, and gardening. His fondest and most vivid medical school experience was holding a retractor for Dr. Henry Royster during an eight-hour neck dissection.

**24 O. Victor Lindelow, M.D.,** retired from internal medicine in January, 2001, after practicing for 46 years in Bismarck, N.D. He became a fellow of the American College of Physicians in 1976. Dr. Lindelow has served as governor of the American College of Physicians for North Dakota and as president of the North Dakota Medical Association. Former chief of medical service at St. Alexius Hospital, he is clinical associate professor of medicine at the University of North Dakota School of Medicine. He has served as chairman of the board of Blue Shield. He and his wife Betty have been married since 1950 and have two sons and two daughters.

**25 Albert A. Lucine Jr., M.D.,** West Chester, Pa., was chairman of the Department of Obstetrics and Gynecology at Chester County Hospital for about





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fifteen years before retiring last year. He and his wife Mary Jane have two daughters, and the entire family has raised and showed a few Morgan horses. Dr. Lucine is a past president and director of the National Morgan Association.

**26 William G. Mays, M.D.,** lives in Tulsa, Okla., with his wife, Ruth. In 1999 he retired from his occupational medicine practice and as instructor at Oklahoma University in Tulsa. He once managed a 25-bed hospital in rural Oklahoma. For many years, Dr. Mays was a part owner of a minor-league baseball team affiliated with the St. Louis Cardinals, and he was a team physician for the Tulsa Oilers baseball team and local high-school teams.

**27 Charles F. Melchor Jr., M.D.,** retired from radiology in 1982 when he suffered a massive stroke. He had spent the previous 25 years in general diagnostic radiology at Decatur Memorial Hospital and Bloomington Radiology in Illinois. Dr. Melchor and his wife Pauline live in Myrtle Beach, S.C.

**28 Edwin W. Monroe, M.D.,** lives in Greenville, N.C., where he sits on the board of trustees of Pitt County Memorial Hospital and enjoys reading, walking, and playing golf. Before his retirement in 1993, he was executive dean at East Carolina University School of Medicine, where he is now emeritus professor of medicine. Dr. Monroe was formerly executive director of the Kate B. Reynolds Charitable Trust. He is a fellow of the American College of Physicians.

**29 Charles F. Montague, M.D.,** and his wife Marilyn met while they were students at Penn; they have been married 55 years and have four daughters. Dr. Montague was associate clinical professor in the Department of Obstetrics and Gynecology at the University of Califor-

nia at Los Angeles and maintained a private practice in Ventura, Calif., for nearly fifty years. Since 1982 he has been active in Aeromédicos, providing medical care to outlying clinics in Baja California and Mainland Mexico; he has also traveled to Kenya and East Africa providing his surgical services. He enjoys flying and sailing and maintains an antique airplane and car.

**30 Bernadine Ziegler Paulshock, M.D.,** retired from internal medicine in 1960. She worked as senior attending and associate program director in the Department of Family Medicine at the Medical Center of Delaware and as associate clinical professor at Thomas Jefferson University. After her retirement, she became editor of the Delaware Medical Journal and became a fellow of the American College of Physicians. She enjoys medical journalism and history and spends a great deal of time reading and writing. Of medical school, she particularly recalls "anatomy with Dr. Williams . . . pharmacology with Dr. Schmidt." Dr. Paulshock lives with her husband Marvin in Wilmington, Del.; they have three children and three grandchildren.

**31 Edward J. Pavsek, M.D.,** lives in Ponce Inlet, Fla., with his wife of 50 years, Adelina. Of their seven children, three hold degrees from the University of Pennsylvania. Dr. Pavsek retired from radiology and nuclear medicine in 1989. He has been a member of the faculty at the University of Pittsburgh, Duquesne University, the University of Pennsylvania, and Penn State. He is the former chair of the Department of Radiology at Mercy Pittsburgh and a fellow of the American College of Radiology. Dr. Pavsek is enjoying his retirement wood-working, fly-fishing, gardening, and baking.

**32 Gerald W. Peskin, M.D.,**

and his high school sweetheart Pearl live in Emeryville, Calif., where he is clinical professor of surgery at University of California at Davis. He serves as associate editor of the Archives of Surgery. He hopes to retire within the next year and spend time with his family; he has three children and five grandchildren. He also enjoys art and golf. Dr. Peskin's most memorable experience at Penn was his first clinical clerkship on the surgical service, with Drs. Koop, Ravdin, and Rhoads.

**33 Rose Pully, M.D.,** lives in Kingston, N.C. After retiring from her private practice in family medicine in 1976, she went on to become a clinical professor of family medicine at East Carolina School of Medicine in Greenville, N.C. Her pediatric experience at Children's Hospital during her third year of school still stands out, and she writes, "I am forever grateful and appreciative of my experience at the University of Pennsylvania School of Medicine."

**34 David G. Rimer, M.D.,** lives in Santa Monica, Calif., with his wife of 15 years, Anne Joy. Until his retirement in 1994, he alternated between his full-time private practice and various academic and directorial positions, including clinical professor of medicine and acting chief of gastroenterology at UCLA Center for Health Sciences and director of the GI lab and chief of gastroenterology at St. John's Hospital in Santa Monica. Still active in medicine, he builds cabinets and furniture in his spare time.

**35 James W. Russell, M.D.,** retired from internal medicine in 1999. He maintained a private practice in St. Johnsbury, Vt., from 1958 to 1992 (he expanded it to a group practice in 1977). Dr. Russell also participated in establishing Founders Hall, a detoxification and primary rehabilitative care program for alcoholics and drug addicts at Northeastern Vermont Regional Hospital. He now lives in Tucson,

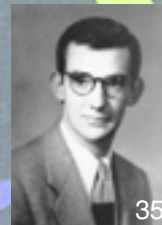
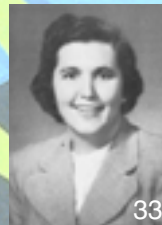
Ariz., with his wife Marilyn. He plans to start work on his memoirs of the Depression and war years, his education and training, and his early practice.

**36 Douglas W. Sanders, M.D.,** lives in Akron, Ohio, with his wife Jane. They have been married for 51 years and have three children. He specializes in internal medicine and was a member of the Council of Summit City Medical Society from 1988 to 2000. He has no plans to retire yet.

**37 Robert T. Schorr, M.D.,** San Diego, closed his general surgery office in 1998, but continues to work as a surgical assistant and hopes soon to publish a piece in a national publication for the fifth consecutive decade. He was inducted into Phi Beta Kappa and Alpha Omega Alpha and received a Bronze Star and a Combat Medical Badge during the Korean War. He recalls his proudest moment at Penn, receiving a letter from Dr. Francis C. Wood in February of 1950 that congratulated him on "one of the best histories it has ever been my privilege to read." He and his wife, Georgene, have been married 23 years.

**38 Bernard Shapiro, M.D.,** Narberth, Pa., specialized in nuclear medicine before retiring in 1998. He worked his way up at the Albert Einstein Medical Center, eventually becoming director of the Radiation Research Laboratory – a position he held for nearly thirty years. He is now a trustee and chairman emeritus in the Department of Radiology there. Dr. Shapiro was a fellow of the American College of Nuclear Physicians. He plans to study digital photography and enjoy retirement with his wife of 51 years, Norma, and their three children and six grandchildren.

**39 Carl M. Shetzley, M.D.,** Doylestown, Pa., and his wife of 53 years, Marion Elizabeth, have four children and five grandchildren. He retired from fami-





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ly practice in 1991, having served as president of Doylestown Hospital medical staff and of the Bucks County Medical Society. Dr. Shetzley was a delegate to the Pennsylvania Medical Society for 20 years. He now enjoys gardening, playing bridge, and working on his genealogy.

**40 Scott Dorsey Skillern, M.D.,** South Bend, Ind., specializes in dermatology but plans to retire soon. He and his wife have four children and two grandchildren. He is an active member of St. James Episcopal Church and plays golf in his free time.

**41 James E. Smith II, M.D.,** Baltimore, practices psychiatry in Towson, Md. He and his wife Patricia have six children.

**42 Irvin H. Sokolic, M.D.,** lives in Princeton, N.J., with his wife of 37 years, Joyce Rochelle. They have six sons and six grandchildren. Dr. Sokolic practiced general surgery for twenty years and maintained a general practice for another twenty. He has received 21 grants and published 16 original papers, has served as director of the surgical residency program at Albert Einstein Medical Center, and was named a fellow of the American College of Surgeons. Now that he is retired, Dr. Sokolic plans to pursue a Ph.D. degree in botany.

**43 Robert Spier, M.D.,** splits his time between Punta Gorda, Fla., and East Aurora, N.Y. He and his wife Mina have four children and three grandchildren. Dr. Spier practiced thoracic surgery until his retirement in 1987; among the positions he held are instructor of surgery at Cornell University and clinical associate professor of surgery at the State University of New York at Buffalo. He plays tennis and golf, goes boating, and travels.

**44 John J. Sprowls, M.D.,** retired from obstetrics and gynecology in 1995. He has served as president of the Rahway Hospital med-

ical staff, as president of the Union County Medical Society, and as chairman of the Committee on Family Life and Sex Education. He is active in the local school board and Rotary Club. He has many memories of Penn – including meeting his wife on campus – and is grateful that he and his classmates were privileged to practice during the “Golden Age of Medicine.”

**45 Edward Colmery Sutton, M.D.,** lives in Burlington, N.C., with his wife Jeanie. In 1989 he retired from obstetrics and gynecology but still volunteers at the Open Door Clinic in Burlington. He has been chief of the medical staff at Memorial Hospital of Alamance, president of the North Carolina Ob-Gyn Society, and chairman of the ob-gyn section of the North Carolina Medical Society. In his free time Dr. Sutton plays golf and gardens.

**46 Edgar H. Ward, M.D.,** Erie, Pa., retired from internal medicine in 1994 but still contributes time to a medical clinic. He enjoys playing golf and gardening. About his medical-school days, he recalls “a great education and clinical experience – superb teachers.” Dr. Ward and his wife Jeanne met at Penn and have been married for fifty years. They have two children.

**47 Allen M. Yeakel, M.D.,** lives in Mount Joy, Pa., with his wife of 49 years, Theresa. They have four children and six grandchildren. Dr. Yeakel retired from anesthesiology in 1990 and plans to spend time studying neurophysiology, growing vegetables, and enjoying music. While practicing, he also taught at West Virginia University and was the founding chairman of the Department of Anesthesiology at Pennsylvania State University College of Medicine. His favorite experience at Penn was participating in summer work with John Lilly and Britton Chance at the Johnson Foundation.



Daniel M. Albert, M.D. '62, left, one of this year's recipients of the Distinguished Graduate Award, is flanked by Stuart Fine, chair of Penn's Department of Ophthalmology.



Edward W. Holmes, M.D. '67, former chair of Penn's Department of Medicine, returned to campus to receive the medical school's highest honor, the Distinguished Graduate Award.

## It Happened One Weekend

Amid the pleasant meals, catch-up conversations, and high-spirited parades down Locust Walk that take place on Alumni Weekend, many returning alumni of the School of Medicine also found time to attend the annual meeting of the Medical Alumni Society. They listened to **Arthur K. Asbury, M.D.**, interim dean, speak about the state of the school, and they saw **Joseph Gordon, M.D. '57**, introduced as the next president of the society. An internist from Drexel Hill, Pa., Gordon received the Alumni Service Award last year, at which time he was described as "the quintessential Penn citizen." Gordon succeeds **Henry A. Jordan, M.D. '62**, who completed his two-year term. Alumni also witnessed the presentation of the school's highest honor, the **Distinguished Graduate Award**. This year, the two recipients were **Daniel M. Albert, M.D. '62, G.M.E. '66**, and **Edward W. Holmes Jr., M.D. '67**.

At the Academy of Music, members of the Class of 2001 acknowledge family and friends for their support.



President Joseph Gordon, left, and Dean Arthur Asbury lead the parade of School of Medicine alumni down Locust Walk.



Albert is internationally renowned as a pioneering researcher, educator, author, and historian in the field of ophthalmology. His six-volume *Principles and Practice of Ophthalmology* is considered the authoritative contemporary compendium of the field.

After earning his M.D. degree from Penn, Albert completed his internship and residency in ophthalmology at HUP. In 1969 he went to Yale University School of Medicine as assistant professor and soon rose to full professor. He joined Harvard Medical School in 1976 and was named the David G. Cogan Professor of Ophthalmology in 1983. Since 1992 he has been chair of the Department of Ophthalmology at the University of Wisconsin-Madison and the Frederick A. Davis Professor of Ophthalmology. Albert has received an honorary degree from L'Université Louis Pasteur in Strasbourg.

Editor-in-chief of *Ophthalmic Surgery: Principles and Techniques* (1998), Albert has served on the editorial boards of nine scientific medical journals. He is currently editor of *Archives of Ophthalmology*. His research focuses on ocular tumors, specifically melanoma and retinoblastoma. He is now investigating the molecular biology of retinoblastoma and whether vitamin D analogs produce tumor regression.

Holmes is widely known as an advocate for the vital role of medical schools in translational medicine – the application of scientific discoveries to the development of better diagnostic methods and treatments. He is also a nationally recognized clinical investigator and molecular biologist specializing in genetics and metabolic disease.

After taking his internship at HUP, Holmes went on to complete his research and clinical training at Duke University Medical Center. He began a steady climb in Duke's academic ranks, eventually becoming chief of the Section of Metabolic and Genetic Diseases and then chief of the Division of Metabo-

lism, Endocrinology, and Genetics. In 1991 he was recruited to Penn as chair of the Department of Medicine. In his six years as chair, the department increased its clinical revenue by 136 percent and raised its ranking in grant funding from the NIH from 22<sup>nd</sup> to 6<sup>th</sup>. Holmes was also a strong proponent of multidisciplinary centers and institutes; four such new programs, with faculty based primarily in medicine, were begun under his chairmanship.

In 1997 he joined Stanford University School of Medicine as the senior associate dean for research and vice president for translational medicine and clinical research. He returned to Duke in 1999 to become vice chancellor for academic affairs of the Medical Center and dean of the School of Medicine. Last fall, Holmes was appointed vice chancellor for health sciences and dean of the School of Medicine at the University of California at San Diego.

Holmes has held continuous NIH funding since 1975, including a M.E.R.I.T. Award. His laboratory has made significant contributions to our understanding of the control of purine biosynthesis. He is currently focusing on a genetic defect linked to congestive heart failure. Holmes is active on the NIH Scientific Boundaries Panel, the scientific advisory board of SmithKline/Beecham, and the National Diabetes and Digestive and Kidney Diseases Advisory Council of the NIH. He has been elected to the American Society for Clinical Investigation, the Association of American Physicians, and the Institute of Medicine of the National Academy of Sciences.

As in previous years, the School of Medicine also presented its Alumni Service Awards. This year's recipients, honored at the Dean's Dinner, were Sylvan H. Eisman, M.D. '41, and Walter J. Gamble, M.D. '57. Eisman was described by Dean Asbury as "a sensitive and knowledgeable physician as well as a committed teacher, . . . a healer in the classic sense. He has embodied

in his career, and has transmitted to countless students, a set of values that emphasizes treating the whole person. And he continues to commit his talents and energies to improving the practice of medicine, addressing the problems of risk management and medical malpractice." Eisman is now Distinguished Emeritus Professor of Clinical Medicine at Penn. He has served the School of Medicine in countless volunteer roles and has contributed many ideas that have shaped alumni events for the better.

Gamble, described by Asbury as a "quiet crusader" who has built support for student financial aid, established the Twenty-First Century Endowed Scholars Program with his wife Anne. As Asbury put it, "His humble and generous nature has endeared him most to the people who are the focus of his attention: Penn medical students. He and Anne have forged strong relationships with the students touched by their generosity."

The Graduation ceremony was held in Philadelphia's Academy of Music, lending some additional glamour and color to the proceedings. One of the speakers was Leon Aller, M.D. '51, representative of the 50 Year Class, an emeritus professor of family practice at the University of Washington, who has devoted much of his professional life to medical mission work. But Aller took the opportunity to liven things up by playing his harmonica, too. Delivering the Graduation Address was Michael S. Brown, M.D. '66, the Nobel Prize recipient who serves as the Paul J. Thomas Professor of Molecular Genetics and Internal Medicine and director of the Jonsson Center for Molecular Genetics at the University of Texas Southwestern Medical School in Dallas. As part of his message to the new graduates, Brown emphasized some important characteristics of a good physician that never change, which can be summed up as CLASS: Compassion, Learning, Astuteness, Skills, and Science. ■

**Progress Notes**

compiled by Erin Hennessy

Send your progress notes to:  
Office of Medical Alumni Relations  
University of Pennsylvania  
Medical Center  
Suite 750  
3535 Market Street  
Philadelphia, PA 19104

**30's**

**Theodore Livingston Hartridge, M.D.** '34, is a retired otolaryngologist in Madison, Wis. He and his wife are members of the American Forestry Association; along with their interests in nature conservancy, they have been actively involved in state and national history research. During the Second World War, Dr. Hartridge served in the Army Medical Corps and received the Bronze Star. He was one of the first American medical officers to examine prisoners in concentration camps at Buchenwald, Cham, and Mauthausen. At Washington University, he was a fellow in otolaryngology while also serving as professor of military science and tactics. Colonel Hartridge served in the Office of the Surgeon General at the Pentagon until 1950, and he also served as chief EENT Surgeon at Brooke Army Hospital in San Antonio. Named a fellow of the American College of Surgeons in 1958, he is a former president of the Society of Otolaryngologists. He was a professor of medicine at Baylor Medical School before joining the Jackson Clinic in Madison; there, he became staff surgeon and a member of the board and president of the Methodist Hospital medical staff.

**50's**

**Ralph Heinz, M.D.** '55, was recently honored with a dinner by the Department of Radiology of Duke University, commemorating his 22

years as professor of radiology and chief of the division of neuroradiology. Earlier, he had been associate professor of radiology at Yale University and chair of radiology at the University of Pittsburgh. While at Yale, he developed the C1-2 spinal puncture for neuroradiology, now used throughout the world. He was the editor of the volume on neuroradiology in the five-volume series *Clinical Neurosciences*. He received a "Best Teacher Award" from Duke in 1988. Dr. Heinz continues to practice in the department part time.

**Norman B. Ackerman, M.D.** '56, Ph.D., has published two books since his retirement from surgery. *Fat No More*, chronicling his experience with morbid obesity, was issued by Prometheus Books. *Morbid/Mortality*, originally published on the web by iUniverse, is a mystery set in a teaching hospital, featuring a third-year medical student as protagonist. Ackerman is currently at work on a sequel.

**Charles L. Greenblatt, M.D.** '56, is preparing the second edition of his book *Digging for Pathogens*. The book, first published (in English) by Balaban Publishers of Israel in 1998, puts ancient diseases into context. He is also presently involved in DNA analyses of thousands of shards from the Dead Sea Scrolls. According to Greenblatt, reassembling individual scrolls from this complex puzzle would be much easier if the pieces can be linked to specific (sheep) parchments.

**70's**

**Mark T. Groudine, M.D.** '75, professor of radiation oncology at the University of Washington School of Medicine, was elected to the National Academy of Sciences. He serves as director of the division of basic sciences at the Fred Hutchinson Cancer Research Center.

**Michael A. Grippi, M.D.** '76, G.M.E. '82, was named chief of medicine at the Philadelphia VA Medical Center and vice chair of Penn's Department of Medicine. A member of the pulmonary/critical-care division, he recently completed a term as medical director of Penn Medicine at Radnor. He is also chair of HUP's Medical Board.

**Theresa Vogel Crouch, M.D.** '79, after living in England with her British husband for almost 10 years, recently accepted a position as a diagnostic radiologist at John Peter Smith Hospital in Fort Worth, Texas. She had worked as a radiologist at RAF Lakenheath, Suffolk, England. She became a member of the Royal College of Radiologists and of the Anglo-American Medical Society and a fellow of the Royal Society of Medicine, all based in London.

**80's**

**David S. Block, M.D.** '86, was named executive vice president of international operations for DuPont Pharmaceuticals. Most recently senior vice president of business development and strategic planning, he joined the company in 1990 and was a major contributor to the successful launching of the anti-HIV medication Sustiva. An assistant professor of medicine at Johns Hopkins Hospital, he also is a member of the attending staff of the Moore Clinic for HIV patients. Dr. Block has an M.B.A. degree from Penn.

**90's**

**Nicholas Abidi, M.D.** '90, was recently appointed an associate editor for *Foot and Ankle International*, and he co-edited the spring issue of *Orthopaedic Clinics of North America*. He has been a fellow of the American Academy of Orthopaedic Surgeons and

chairman of the young physicians section of the American Orthopaedic Foot & Ankle Society. Abidi serves as attending physician at Dominican Hospital in Santz Cruz, Calif., and is the team physician for the University of California at Santa Cruz, Bethany College, and several local high schools.

**Eric Britton, M.D.** '96, recently completed his training for general practice in the British National Health System and has been offered a partnership in the James Wigg Partnership, a large teaching practice in North Central London. As part of his duties, Britton will be responsible for educating students from University College London Medical School. He can be reached by e-mail at eric.britton@ukgateway.net or ericbrittonmd@hotmail.com.

**OBITUARIES**

**H. Corwin Hinshaw Jr., M.D.** '33, Belvedere Tiburon, Calif.; December 28, 2000. He served as head of the Section of Medicine at the Mayo Clinic Foundation, University of Minnesota, from 1947 to 1949, then moved to California to practice internal medicine. In 1952, he and collaborator William Feldman were nominated for the Nobel Prize in Medicine for their successful treatment of tuberculosis patients with streptomycin. He went on to become an emeritus professor at the University of California School of Medicine at San Francisco.

**James H. Farrior, M.D., G.M.** '36, Iowa City, Iowa; April 11, 1996.

**John H. Prewitt, M.D.** '36, Lexington, Ky.; December 1, 2000.

**Louis Udell, M.D.** '36, Philadelphia, retired rheumatologist and instructor; February 4, 2001. He was an instructor at Penn from 1950 to 1974; he



also had a private practice in Northeast Philadelphia and was a staff physician at Nazareth and Lower Bucks hospitals. He collaborated on an early study using cortisone injections to treat arthritis. Dr. Udell was a fellow of the American College of Rheumatology.

**Calvin P. Wallis, M.D.** '36, Duarte, Calif.; June 28, 2000.

**Charles Fletcher Owen, M.D.** '37, Asheboro, N.C., retired radiologist; January 6, 2001.

**John Lockwood Morrison, M.D.** '38, Waltham, Mass., obstetrician and gynecologist; February 9, 2001. During World War II, he served in the Medical Corps, 55<sup>th</sup> General Hospital, stationed in Europe. In 1998, the Massachusetts Medical Society honored him for his 50 years of membership.

**Oliver William Suehs, M.D., G.M.E.** '38, Austin, Texas, a retired otolaryngologist who had maintained a practice there for 35 years; January 2, 2001. During World War II, he was chief of the otolaryngology department at the 127<sup>th</sup> General Hospital unit in Europe. A former chief of staff at St. David's Hospital, he had served as president of the Travis County Medical Society, as vice president of the otolaryngology section of the Texas Medical Association, and as vice president of the American Laryngology Association.

**Birna Nystrom Sullivan, M.D., G.M.** '38, Green Valley, Ariz; Autumn 2000.

**Eugene S. Bereston, M.D., G.M.** '40, G.M.E. '55, Pikesville, Md., clinical professor of dermatology at the University of Maryland and chief of dermatology at Mercy Hospital in Baltimore; December 16, 2000. He was team dermatologist to the Baltimore Orioles and the old Baltimore Colts.

**Floyd M. Landis, M.D.** '40, Leola, Pa., a retired physician; February 5, 2001. He

served his internship at Lancaster General Hospital. Starting his family practice less than two miles from the farm where he was born, he practiced until 1986. A medical officer during World War II, he was a major in the U.S. Army and served at an evacuation hospital in Europe. Landis, who played clarinet and saxophone, was a charter member of the New Holland Boys Band. In 1990, the Lancaster City and County Medical Society honored him on the 50th anniversary of his graduation from medical school.

**Edwin W. Cauffield, M.D., G.M.** '42, Akron, Ohio; June 3, 2000.

**Victor J. Montilla, M.D., G.M.** '42, Fayetteville, N.C.; June 4, 1994.

**Joseph S. Burkle, M.D.** '43, G.M. '50, York, Pa.; December 2000.

**William F. McGuire, M.D.** '43A, Wichita, Kan.; May 27, 1999.

**John J. Angelo, M.D.** '44, York, Pa.; January 23, 2001.

**Carl W. Filsinger, M.D.** '44, Stone Harbor, N.J., retired physician; February 1999.

**Herbert S. Greenspan, M.D., G.M.** '45, Jenkintown, Pa., retired pediatrician and child psychiatrist; December 24, 2000. He had a private practice and later served as head of the children's psychiatric clinic at Abington Memorial Hospital. He also volunteered at the Philadelphia School for the Deaf & Dyslexic and at Martin Luther King High School.

**Hiram L. Wiest, M.D.** '45, Hershey, Pa., a retired professor of family and community medicine at Milton S. Hershey Medical College; January 11, 2001. After earning his medical degree, he trained as a general-practice intern at Lancaster General Hospital, then served as an officer in the U.S. Army Medical

Corps. From 1948 to 1966, Wiest practiced family medicine in his hometown of East Petersburg, Pa. At Hershey Medical College of Penn State University, Wiest helped establish a curriculum in family medicine and helped found the Department of Family and Community Medicine. He was a former president of the Pennsylvania Academy of General Practice. He retired from Hershey in 1981. Active in community education, he served as president of the Hempfield Union and Lancaster County school boards.

**Robert Buch, M.D.** '46, Mountville, Pa.; February 7, 2001. He had a family practice in Mountville for 30 years and also served as deputy coroner of Mountville and West Hempfield Township. During World War II, he served as a captain in the Army Air Forces Medical Services.

**Alfred H. Dobrak, M.D., G.M.** '46, Pompano Beach, Fla.; January 26, 2001. He was an Army captain in World War II, serving in the European Theater. In 1948, he became certified by the American Board of Radiology. He practiced at Sisters Hospital and the former Emergency Hospital in Buffalo, N.Y., before moving to Florida.

**Charles Herrick Knickerbocker, M.D.** '46, Bar Harbor, Maine; January 9, 2001. Since 1947, he served the Mount Desert Island community as a family physician specializing in internal medicine and cardiology. A chief of staff and medical review officer for the Mount Desert Island Hospital, he had been president of the Hancock County Medical Society. He also wrote several novels, including *The Dynasty*, *Summer Doctor*, and *The Hospital War*.

**Henry Albert Segal, M.D.** '46, Chevy Chase, Md., psychiatrist and psychoanalyst; January 12, 2001. He did his psychiatric residency at Walter Reed Army Medical Center. From 1946 to 1955, he was

in the Army Medical Corps, which included service in the Korean War. He retired as a major, and his decorations included the Legion of Merit and the Bronze Star. Since the 1960s, Segal had worked on and off at the Washington School of Psychiatry, where he taught classes in advanced psychotherapy training and professional identity issues. He had also been affiliated with the Georgetown University School of Medicine, where he taught a course in communication skills for medical students.

**Louis Magilner, M.D., G.M.** '47, Delray Beach, Fla.; June 20, 2000.

**Richard P. Ornstein, M.D.** '47, Gladwyne, Pa; December 28, 1999.

**John R. Higgins, M.D., G.M.** '48, Floyds Knobs, Ind.; February 2001.

**David R. Patrick, M.D., G.M.** '48, Beaver, Pa.; November 29, 1992.

**Blair W. Saylor, M.D., G.M.** '49, Tucson, Ariz.; May 12, 2000.

**Robert Greenleaf Umstadd, M.D.** '49, Beckley, W.Va., retired anesthesiologist; June 14, 2000. He served as a United States Navy Lieutenant in the Korean Conflict, practicing family medicine and surgery for two years before returning to the United States for an anesthesiology residency at Mary Hitchcock Hospital at Dartmouth, N.H. He then returned to Austin, Texas, where he grew up; in 1957, he joined the Austin Anesthesiology Group. Dr. Umstadd was instrumental in advancing outpatient surgical centers, notably Bailey Square Surgical Center.

**Paul E. Maust, M.D.** '50, Butler, Pa.; January 21, 2001. After maintaining a family practice in Petrolia for seven years, he entered a four-year residency in general surgery at the Philadelphia Veterans Hospital; during this time he

also pursued graduate work in pediatrics at The Children's Hospital of Philadelphia. He then practiced surgery for 30 years in Butler, serving as chief of staff at Butler Memorial Hospital and president of the Butler Medical Society.

**Robert H. Thomas, M.D.** '51, Yakima, Wash.; September 5, 2000.

**Ralph M. Brugger, M.D.** '52, Ames, Iowa; August 9, 2000. He practiced at the McFarland Clinic for 33 years.

**Hadley L. Conn Jr., M.D., G.M.E.** '53, Piscataway, N.J., emeritus professor and chair of the Cardiovascular Institute of the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School; Dec. 3, 2000. He was a former professor of medicine at Penn.

**Ben P. Estes, M.D., G.M.** '53, Philadelphia; October 14, 1998.

**David Kasner, M.D., G.M.** '56, Coral Gables, Fla.; January 6, 2001.

**Willard F. Conger, M.D.** '74, San Francisco; October 1995.

## FACULTY DEATHS

**Hadley L. Conn Jr., M.D.** See Class of 1953.

**James Joseph Ferguson Jr., M.D.,** Chevy Chase, Md., former chair of biochemistry and former associate dean; February 17, 2001. After earning his medical degree from the University of Rochester, he took an internship and a residency in endocrinology at Massachusetts General Hospital. He came to Penn in 1959 with a dual appointment in biochemistry and medicine (endocrinology). A Markle Foundation scholar, he received a research career development award from the NIH. He became a

full professor in both departments in 1971; was director of the endocrinology section in the Department of Medicine from 1966 through 1969; and served as chairman of biochemistry from 1971 to 1975, at which point the biochemistry department was merged with biophysics. He was appointed associate dean for special programs in 1975, a position he held until 1986, and he served on many advisory committees both here and at the NIH. Ferguson's research centered on the molecular basis of hormonal action; an important contribution was demonstrating the value of photoaffinity labeling in such studies. He was also a flutist with the Philadelphia Doctors' Orchestra, which he served as president. After leaving Penn, Ferguson spent seven years at the National Library of Medicine in Bethesda, Md., where he was involved with the design of a biotechnology database.

**R. Claude Rogers, M.D.,** Bala Cynwyd, Pa., emeritus assistant professor of physical medicine and rehabilitation; December 15, 2000. Educated in Bucharest, he came to the U.S. in 1964. He joined Penn in 1971 as an instructor and became an assistant professor in 1978. He retired in 1988. An artist himself, Rogers believed that art could play a role in healing mind and body, and he published a book on the subject. His own art was displayed in local galleries, including Penn's Faculty Club.

**Robert Stanek, M.D., G.M.E.** '77, Huntingdon Valley, Pa.; December 31, 2000. After receiving his medical degree from Temple University in 1972, he went on to serve his residency at Rhode Island Hospital at Brown University. He served on the staff at Frankford Hospital, Holy Redeemer Hospital, and HUP. He was a fellow of the American College of Surgeons.

**Louis Udell.** See Class of 1936.

## Gottlieb's Gift



**P**hilip M. Gottlieb, M.D.'35, believes in giving credit where credit is due. In private practice in internal medicine and allergy for more than 40 years, he played a major role in persuading the American Medical Association to move allergy to its own section (he served as founding chair) and to include it as an independent field in the American Board of Medical Specialties.

Today, Gottlieb takes pride in the fact that allergy "gets its due." But he's still pushing for recognition of people and institutions that make important contributions. This time around, his focus is his alma mater.

"In all those years of practice, I kept thinking back to the fine training I had in medical school and my professors," he says, citing Truman Schnabel Sr., I. S. Ravdin, and Charles C. Wolferth. "I just felt I ought to give back some token of what they did for me." In January, he did — honoring the School of Medicine by establishing a charitable gift annuity.

Inspired by his three physician uncles, Gottlieb planned a career in medicine from the start, enrolling in Penn's special seven-year undergraduate/medical degree program. "I did it just to save a year and get to work," he says. A Simon Muhr scholarship paid his \$400-per-semester tuition. Gottlieb graduated Phi Beta Kappa and served as editor of the Class of '35 Record.

His professional highlights include induction into Alpha Omega Alpha and teaching appointments at HUP and Philadelphia General Hospital. He served on two NIH consensus development committees and chaired one of them. He was a director of the American Board of Allergy and Immunology as well as president of the American College of Allergists and Immunologists. Following a heart attack in 1981, he sold his practice.

A frequent visitor to Penn, Gottlieb approves of the many changes he's seen. His gift, he says, is also a form of thanks for the special status he enjoyed: "When you circulate around doctors in the country, you discover that the title 'Penn graduate' is very highly regarded."

In addition to obtaining a generous income tax deduction, Gottlieb will receive a lifetime income stream from the charitable gift annuity. His planned gift is just one of the creative gift opportunities that would benefit both the School of Medicine and its alumni. As you chart your financial future, the Planned Giving Office is ready to assist in developing an appropriate strategy. **Contact Marcie Merz, J.D., director of planned giving, University of Pennsylvania Medical Center, 3535 Market Street, Suite 750, Philadelphia, PA 19104-3309. Phone: 215-898-9486. E-mail: mmerz@ben.dev.upenn.edu.**

### A Campaign Concludes

One of the most satisfying duties during my year as interim dean was observing the wonderful progress made by the School of Medicine's capital campaign. The Creating the Future of Medicine campaign was launched in the fall of 1995, and it was my pleasure to preside at an event this past April that celebrated its official close. There was indeed much to celebrate. The total raised in those five years is a tribute to all our donors and volunteers: \$648 million for education, research, and patient care. We had an amazing 42,000 donors, and the average gift was about \$14,000.

Among alumni, the average gift was \$8,469. I am happy to point out that Penn medical alumni have always answered the call for support during capital campaigns. We can trace this support back some 130 years, when a young clinical lecturer named William Pepper Jr. led alumni in a three-year campaign to raise \$700,000 to establish the Hospital of the University of Pennsylvania.

Recruiting and retaining the finest faculty has long been a priority at Penn. As the Ruth Wagner Van Meter and J. Ray Van Meter Professor Emeritus of Neurology, I know at first hand how valuable the support provided by endowed chairs is to our faculty members. In the course of the campaign, 45 endowed chairs were created in the school.

The endowment for financial aid showed an astonishing growth: from \$37 million in 1989 to \$127 million in 2000. One reason for the increase is that student financial aid was one of the campaign's priorities – but in addition, the School of Medicine had several alumni and friends who served as champions of financial aid. Two couples deserve special mention, the Gambles and the Welshes. Raymond H. Welsh, a trustee of our Health System and a 1953 alumnus of the Wharton School, chaired the entire campaign. In addition, he and his wife, Joanne, launched the Welsh Faculty Challenge, by which they matched every gift of \$1,000 or more from a member of the faculty, up to a total of \$1 million. In all, the Faculty Campaign Committee helped to



secure gifts from more than 250 faculty members in support of student financial aid. Including matching funds put up by the Welshes and by Walter J. Gamble, M.D. '57, and Anne Gamble, close to \$4 million was generated by faculty giving. It was an honor for me to serve as chair of that committee.

No overview of the capital campaign would be complete without a salute to the Gambles. They created the visionary Twenty-First Century Endowed Scholars program to relieve the increasing debt burden shouldered by most medical students. After their initial gift of \$10 million to create full-tuition scholarships, they have continued over the years to support financial aid through gifts of an additional \$17 million. For example, they established the Gamble Challenge to alumni donors at the \$25,000 level, and 58 alumni responded.

Albert M. Kligman, M.D., Ph.D., is both an alumnus of the School of Medicine (Class of 1947) and an emeritus faculty member in our Department of Dermatology. He and his wife Lorraine H. Kligman, Ph.D., pledged \$1 million in support of the Twenty-First Century Endowed Scholars program. There are many other supporters, too numerous to name here, but all of them have our profound thanks.

I would also like to thank the Campaign Steering Committee, including members from our Health System's Board of Trustees, for providing essential oversight of the campaign, for keeping us on track, and for providing stewardship on special projects. Among our alumni, the National Alumni Council made great contributions to the capital campaign in terms of gifts, loyalty, and wise counsel. I want to acknowledge its tireless chairman, Stanley J. Dudrick, M.D.'61.

Still, while we celebrate the tremendous success of the Creating the Future of Medicine campaign and all it will continue to make possible, many challenges remain. Our development efforts continue because there are always fund-raising needs in an institution as large, complex, and forward-looking as ours. Our new executive vice president and dean, Dr. Arthur Rubenstein (see "Vital Signs"), will be setting the priorities in conjunction with Krista Mattox and her expert staff in the development office, but some needs stand out. A plan is under way to upgrade the school's educational facilities and cluster them in the John Morgan Building and adjacent parts of the Anatomy-Chemistry Building. This is a major project, and there are others. We need better connections and access between the parts of the Health System on the old site of Philadelphia General Hospital and the rest of the medical campus.

In the area of health services, the operating rooms and the perioperative acute-care units have to be upgraded and expanded, particularly at HUP. Capital intensive upgrades are also necessary at Pennsylvania Hospital, Presbyterian Medical Center, and Phoenixville Hospital. Further, we have a desperate need for an ambulatory care center on campus. Another opportunity is to develop more comprehensive capabilities in the University of Pennsylvania Cancer Center; a particularly attractive possibility is a state-of-the-art proton-beam facility.

It is still too early to measure the full impact of the Creating the Future of Medicine campaign – by definition, the future lies ahead. But we are confident that the impact will be measured in new advances made in research, in the world-class physicians trained in our tradition of excellence, and in the number of lives saved and restored through our patient care. On behalf of this great institution, I extend my sincerest thanks to all who have contributed to our campaign to create the future of medicine.

Arthur K. Asbury, M.D.  
*Interim Dean, School of Medicine*



Charles P. O'Brien, M.D., Ph.D., professor of psychiatry at Penn, has been director of the Treatment Research Center since its founding in 1971. The center has always sought to combine treatment for addiction with scientific research – among other reasons, as he puts it “to try and find out whether treatment A was better than treatment B.” During those 30 years, research into the neurochemistry, neuropsychology, and genetics of drug addiction has changed the way scientists understand addiction and has led to a new generation of drug treatments.

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