



# yale medicine

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restaurants

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learned in Uganda

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# WINTER 2008

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During their rotations in Uganda, residents and medical students visited camps for internally displaced persons. Fighting between the government and the Lord's Resistance Army has displaced hundreds of thousands of people in northern Uganda, such as these boys at the Patiko-Ajulu camp.

### BACKGROUND

Majid Sadigh examined a patient in a neighborhood on the outskirts of Kampala, Uganda's capital. House calls to outpatients of St. Stephen's Hospital are part of the rotations for attendings and medical students.

*Photographs by John Curtis*

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### On the Web

[yalemedicine.yale.edu](http://yalemedicine.yale.edu)

On our website, readers can submit class notes or a change of address, check the alumni events calendar, arrange for a lifelong Yale e-mail alias through the virtual Yale Station and search our electronic archive.



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### Yale should produce more primary care physicians

I would be truly impressed if Yale pursued the path of producing more primary care physicians. As a “liberal” institution of higher learning, where is the responsibility? Lifestyle is important but that was not what medicine was or is about. As for an ophthalmology attending seeing 40 to 60 patients in 10 hours, I am speechless. Who is teaching?

*Harvey Davis, M.D., HS '69  
Virginia Beach, Va.*

### Primary care is vanishing as a practice model

Regarding “Taking the E-ROAD” [*Yale Medicine*, Autumn 2007], I’d like to tell the academics who decry the decline in the number of primary care physicians why I left primary care in 1968. It had nothing to do with lifestyle or economics. I didn’t leave primary care, primary care left me.

The whole practice model was disappearing. I lay awake nights wondering what to do and told my patients that if they could scare up 1,500 families who would let me deliver their babies, treat their fractures, take care of their kids, etc., then I would stay. This was a feeling shared by many of my contemporaries. But the climate was rapidly changing and the academics were clueless as to the reasons. Family practice disappeared, never to return. The change wasn’t just within the medical community but in American society as a whole. As an example, house calls didn’t disappear because physicians wouldn’t make them but because people stopped asking for them.

The young doctor who wrote the article has never been exposed to one generalist supervising care. The medical school hospitals I am familiar with (Yale, where I went to medical school, and Dartmouth, in the area where I now live) have simply never had that model. And I don’t know that they can.

Following my wife’s surgery, a serious post-op problem was handled without talking to her family. Consults were gotten, care discussed and treatment ordered without talking to the patient’s spouse or family doctor until, after four days, in desperation, the husband (me, an M.D.) insisted the primary care M.D. be called. With his background knowledge the primary care M.D. corrected the problem immediately. When I protested the lack of communication I discovered that the primary care M.D. had no privileges even though he is part of the Dartmouth-Hitchcock Medical Center system. I have yet to be talked to by anyone but the intern—even three years later! Today’s medical student never sees the kind of practice that was once so common in community hospitals. He or she has no role model, a fact that is sad but true. The current primary care model bears no resemblance to what I knew and the modern version is no replacement.

*Robert P. Gerety, M.D. '52  
White River Junction, Vt.*

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## Lessons from Uganda

When I returned from Uganda in July, people who asked about my reporting trip to Mulago Hospital assumed that the Yale attendings and residents had gone there to teach. It would seem to make sense that professionals coming from one of the leading universities in the richest country in the world and with access to the latest medical technologies would have much to teach the doctors and medical students at a hospital in one of the world's poorest countries. In fact, the reverse was often true. In the middle of one Yale doctor's first day on the wards at Mulago, he lamented how ineffectual he felt. Said Sam Luboga, M.D., deputy dean of the Faculty of Medicine at Makerere University in Kampala, "When people come here they can really feel bewildered. They find a hospital full of patients, without drugs, without supplies."

At Mulago the Yale doctors became the students, with a lot to learn from their Ugandan colleagues. Denied all the accoutrements of modern medicine that are part of their daily lives, the Yale physicians fell back on the most basic tool of medicine—the physical exam—at which the Ugandan doctors excel. This is not to say that the Yale doctors had nothing to offer. While at Kampala, the Yale attendings and residents taught evidence-based medicine and provided new

models for interactions with patients. The collaboration has also brought to Uganda textbooks and access to electronic medical texts. Both Makerere University and Yale University stand to benefit from the collaboration, which is expected to improve clinical care in New Haven as well as in Uganda.

In this issue we also feature profiles of two doctors who specialize in the heart. John A. Eleftheriades, M.D. '76, HS '83, chief of cardiothoracic surgery, learned the basics of cardiology from Lawrence S. Cohen, M.D., HS '65. The two started as student and mentor, became colleagues and are now co-authors of a book about the heart, *Your Heart: An Owner's Guide*.

On November 30 we learned of the passing of Nicholas P.R. Spinelli, M.D. '44, a warm, kind and generous man and a good friend to all of us at *Yale Medicine*. When we were next door to the Office of Alumni Affairs, he often took the time to chat with us and ask us what stories we were working on or to suggest ideas for articles. And he always had something nice to say about our latest issue. We will miss him.

John Curtis  
*Managing Editor*

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### SECOND OPINION BY SIDNEY HARRIS



## Biotech spinoffs fuel New Haven economy

2007 was a banner year for startup companies based on discoveries in Yale labs.

“Restaurants. Good restaurants.” The surge in upscale eateries opening in New Haven, said Jon Soderstrom, PH.D., managing director of the Office of Cooperative Research (OCR), is one way of gauging Yale’s efforts to build up the local biotechnology industry. When a decade ago Yale made its commitment to create new business ventures based on laboratory discoveries, city gourmets could point to fewer than a handful of top-flight restaurants. Today diners have more than a score to choose from, and Yale’s head of technology transfer thinks much of the credit belongs to biotech.

“Biotechnology has made a substantial difference in the economic climate of the city,” said Soderstrom. Investment

in new and existing Yale ventures reached its highest level yet during the 2007 fiscal year that ended on June 30.

According to OCR’s year-end report, outside investors provided close to \$70 million in fiscal 2007 to launch seven companies based on Yale discoveries. Bioscience companies already in the region secured around \$400 million in new cash for operations. That’s on top of more than \$1.5 billion in private biotechnology investment to date, a portion of it going to the 25 new companies established by the OCR.

Among the newly launched companies was BioRelix, which will develop antibiotics based on discoveries about bacterial RNA targets made in the laboratory of Ronald R. Breaker, PH.D., the Henry Ford II Professor of Molecular, Cellular and Developmental Biology and professor of molecular biophysics and biochemistry. The company received nearly \$26 million from investors. Existing company Achillion Pharmaceuticals received \$52 million

from its initial public offering, part of which will fund development of an antiretroviral therapeutic based on work done by Yung-Chi “Tommy” Cheng, PH.D., the Henry Bronson Professor of Pharmacology.

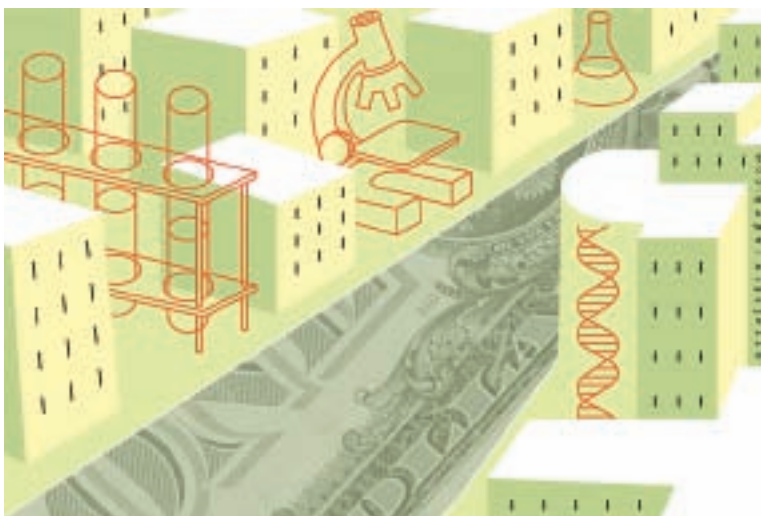
Achillion is one of numerous young companies based in 300 George Street, a former telephone company office building now converted to laboratory space. The building’s nine floors are nearly full, and private developers are planning to construct a new building nearby for biotechnology companies.

Venture capital firm CHL Medical Partners has already invested more than \$25 million in eight Yale spinoff companies. CHL partner Jeff Collinson, a 1963 Yale College graduate, recalls that before OCR began its push few laboratory facilities existed for fledgling companies and his firm had to look outside the region for experienced executives and skilled labor. Now, he said, “biotechs have good laboratory facilities ready to move to New Haven and there’s a pretty good labor pool to recruit from, so it’s much easier to get a company started.”

Said Paul R. Pescatello, J.D., PH.D., president and CEO of CURE, an organization supporting bioscience in Connecticut: “I travel to meetings around the world. My sense is that qualitatively Yale is regarded as highly as any academic medical center in the world” for developing biotechnology enterprises. But quantitatively the region lags, he said, behind Cambridge, South San Francisco, San Diego and other areas with more prominent biotechnology sectors. Those areas, he said, have “other engines” to generate new ventures, while New Haven relies almost solely on Yale.

Soderstrom agreed: “New Haven is an emerging phenomenon. We’re a work in progress. But 10 years ago it was hard to get venture capitalists to come to New Haven. Today they’re here all the time.” And new restaurants keep opening.

—Marc Wortman



## Eyeing “broader impacts,” Yale bolsters efforts to bring science to local schools

High school students in New Haven and neighboring communities are reaping benefits from a federal effort to encourage them to study science and engineering. Because fewer college undergraduates and graduate students are pursuing careers in the sciences than in the past, national organizations are asking researchers to help recruit the next generation of scientists. According to Kathie L. Olsen, PH.D., deputy director and chief operating officer at the National Science Foundation (NSF), the percentage of students remaining in science and engineering after obtaining a master’s degree dropped from 23 percent in 1995 to 15 percent in 2003.

The NSF believes that if science were brought into the classroom and presented by scientists in a compelling way, more students might choose careers in

science. NASA and other major funding sources, including the National Institutes of Health, have followed the foundation’s lead. As a result, since 2002 the NSF has required scientists to include a community outreach plan or a “broader-impact” component in their grant applications.

Yale faculty, staff and students were already running science outreach programs that brought more than 10,000 New Haven young people into free Yale-sponsored programs each year. The NSF broader-impact requirement meant that hundreds more researchers would be getting involved in science outreach.

Claudia R. Merson, the public school partnerships director in Yale’s Office of New Haven and State Affairs, said reaction to the NSF initiative was immediate. “Suddenly, researchers were approaching us saying, ‘I want to do some outreach. What can I do?’ ” Yale responded by convening a science outreach advisory committee that recommended appointing a coordinator for community programs.

Joanna Price, PH.D., whose degree is in molecular biology and biotechnology, took on the job earlier this year. Her goal is to support and expand the many science education programs being offered. She will help faculty members interested in science outreach identify potential partners within the university as well as

in the community; facilitate information and resource-sharing among the university’s science outreach programs; and serve as a liaison to area schools. A new website, [www.yale.edu/scienceoutreach](http://www.yale.edu/scienceoutreach), lists all of Yale’s science programs available for the public.

So far Price has helped with four grant applications and launched a number of initiatives, including a series of talks at Hill Regional Career High School. She’s also working on a \$1 million project to enhance science education in public schools, a program undertaken as part of the university’s purchase of the Bayer facility in neighboring Orange and West Haven.

Price’s position is funded by the provost’s office, the Howard Hughes Medical Institute and the NIH and has the support of existing Yale science outreach programs and from the Yale University Peabody Museum of Natural History.

Now that Yale has a conduit between researchers and K-12 educators, Merson is confident that up-to-date information on a full range of science-related topics will reach and excite the scientists of tomorrow. “We have always had amazing people here doing world-class research,” she said. “Now we have an organized way to share that with the community.”

—Jennifer Kaylin

## YALE SCIENTIST TAPPED TO LEAD WELLESLEY COLLEGE

H. Kim Bottomly, PH.D., a renowned immunobiologist and a deputy provost at Yale, became the 13th president of Wellesley College in Massachusetts in 2007. As deputy provost, Bottomly led an initiative to add women and minorities to the Yale faculty. As a scientist she focused on factors that influence the initiation of immune responses. She has served as a member of the Immunobiology Study Section of the National Institutes of Health and was appointed to the Advisory Council of the National Institute of Allergy and Infectious Diseases.



MICHAEL MARSILAND

## New building on Amistad Street: a place “where great science is done”

Taking a page from theoretical physics, scientists at the School of Medicine’s newest building will shorten the distance between two places—the bench and the bedside. “This is the future,” declared President Richard C. Levin at the October 5 ribbon cutting—a future shaped by interdisciplinary teams quickly translating basic science into clinical solutions.

The 120,000-square-foot building at 10 Amistad Street will house three programs—the Interdepartmental Program in Vascular Biology and Therapeutics, the Human and Translational Immunology Program and the Yale Stem Cell Center. These programs, each of which draws on faculty throughout the university, were identified as crucial to the medical school’s strategic plan, said Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. A lack of lab space, for example, had limited growth in vascular biology. The stem cell center needed facilities after Haifan Lin, P.H.D., a leading researcher, was

recruited to initiate the program with the help of a \$7.8 million grant from the state of Connecticut. And, Alpern said, the new facilities will “capitalize on our incredible strength in immunology.”

The \$88.6 million structure is the latest to be built under a \$1 billion plan to expand science facilities at Yale. The dedication came just as the university acquired 550,000 square feet of laboratory space at the Bayer HealthCare Company’s former headquarters in West Haven.

With workstations for more than 250 scientists, the building on Amistad Street offers sophisticated microscopy and technology for cell sorting and is environmentally sustainable. Designed by Herbert S. Newman and Partners, a New Haven-based firm, with lab spaces planned by Ellenzwieg Associates of Cambridge, Mass., the building features lights that turn off automatically, rainwater collection and other green features.

The day began with a symposium on translational and regenerative medicine. Salvador Moncada, M.D., P.H.D., D.S.C., director of the Wolfson Institute for Biomedical Research,

University College London, spoke on the role of nitric oxide in regulating mitochondria and cell bioenergetics. Douglas A. Melton, P.H.D., co-director of Harvard University’s Stem Cell Institute, outlined his research into the growth and development of pancreatic cells in humans and other vertebrates. Marc Feldmann, F.MED.SCI., director of the Kennedy Institute of Rheumatology at Imperial College, London, gave a talk with an intriguing title, “Anticytokine Therapy: An Approach to All Unmet Medical Needs.” Feldmann and his colleagues proved that anticytokine therapy, which targets the overproduction of hormone-like proteins that regulate the body’s immune response, is effective in treating rheumatoid arthritis and other autoimmune diseases. “Every disease has its cytokine irregularities, and there should be therapeutic targets,” Feldmann said.

Feldmann’s vision of dramatically improved human health was endorsed by speaker after speaker, including Provost Andrew D. Hamilton, P.H.D. “This is going to be a place where great science is done,” he said.

—Colleen Shaddox

From left, Andrew Hamilton, Richard Levin, Robert Alpern, Jordan Pober, William Sessa and Haifan Lin marked the official opening of the new research building on Amistad Street in October. The 120,000-square-foot building will house Vascular Biology and Therapeutics, Human and Translational Immunology and the Yale Stem Cell Center.



TERRY DAGRADI



## Summer program brings high school students into Yale labs to do research

Four years ago Gil G. Mor, M.D., associate professor of obstetrics, gynecology and reproductive sciences, was thinking of ways to get local high school students interested not just in science but also in studying science at Yale.

"Kids in the area would never apply here," he said. "They always think Yale is something belonging to a completely different world. And then there's a decrease in the number of these young kids going into science and medicine."

So Mor initiated the Discovery to Cure program, which brought six high school juniors into Yale research labs that summer. The same year, Mor also asked teachers at the participating high schools how many of their students planned on applying to Yale. The answer was zero. But last year four students in the program applied to Yale, and two are now attending. Other program graduates went on to study science and medicine at such schools as Harvard, Cornell and the University of Chicago. Some have returned to Yale for summer research as undergraduates. Last summer, the fourth year of the program, 20 students spent six weeks in Yale labs.

The new program joins other Yale initiatives to bring high school students into research labs. For several years students at New Haven's Hill Regional Career High School have lived on campus in a summer program during which they participate in small-group problem-based learning. And the Anatomy Teaching Program has brought Career students to the anatomy lab for sessions led by medical students.

"We were a little afraid of bringing teenagers into the lab," Mor said. "They might break things, damage things. But the opposite happened. They contributed to the lab. The work that they did was outstanding."

Kaitlin Markoja from Cheshire High School studied the connection between the immune system and pregnancy in



**At Science Day last summer, high school students in the Discovery to Cure program presented their work. "During four hours we were able to enjoy the capacity of these young minds to acquire, digest and transmit complex concepts," said Gil Mor, the program's director.**

Mor's lab. "People who are pregnant don't respond to viruses in the same way as other people, and we're trying to understand this," she explained.

Markoja's summer research cemented her plans to pursue a career in science or medicine. "It was such a hands-on experience," she said.

Irene Visintin, a research associate who coordinates the program with Mor, said complete immersion is what makes this opportunity so remarkable. "We don't want them in there washing dishes. That's not the goal," she said. Not only do the students contribute to research, but they also remind some of the more senior researchers why science is fun. "They ask a million and one questions and run around smiling," Visintin said.

Kelsey Hogan, a budding neuroscientist from Mercy High School, a parochial school in Middletown, Conn., worked in the lab of Tamas L. Horvath, D.V.M., PH.D., professor of comparative medicine, of neurobiology and of obstetrics, gynecology and reproductive sciences. She studied the effects of maternal obesity on mice offspring, spending most of her days dissecting brains to look for dye that indicated the activity of cells that control appetite.

This gory and repetitive work could turn some people away from science. But Kelsey loved it. "This was the best summer vacation I've ever had," she said, grinning.

—Sarah C.P. Williams

## et cetera ...

### STRESS AND ADDICTIONS

Yale researchers have received \$23 million from the National Institutes of Health to study how stress fuels addictions. They hope to understand why some people stick their hand in a cookie jar, smoke a cigarette or gulp cocktails when they're overworked, have family conflicts or can't balance their responsibilities. These studies could lead to new ways to combat the cravings of addiction and improve control over excessive smoking, drinking and eating.

"Stress is the kind of topic that really begs for being studied in an interdisciplinary way, because it affects every organ system in some way or another," said Rajita Sinha, PH.D., professor of psychiatry and leader of a research consortium that will include psychiatrists, neuroscientists, social psychologists and communications and policy experts.

They will analyze the ways in which events early in life shape a person's ability to handle stress; use neuroimaging to illuminate changes in the brain under stress; and explore the effects of pharmacological agents on stress and on lapses in self-control over such addictive behaviors as smoking, drinking alcohol and overeating. The consortium will also organize population-based studies as well as genetic analyses of vulnerability to stress-related addictive behaviors.

—S.C.P.W.

### YNHH AMONG BEST IN NATION

Yale-New Haven Hospital has been included in the 2007 "America's Best Hospitals" rankings published in July by *U.S. News & World Report*. The hospital was rated among the best in the nation in 10 of the 16 medical specialties evaluated: cancer; digestive disorders; ear, nose and throat; endocrinology; gynecology; heart and heart surgery; kidney disease; psychiatry; respiratory diseases; and urology.

"This recognition is a significant benchmark for Yale-New Haven Hospital as to where we are among the nation's best health care providers," said Peter N. Herbert, M.D. '67, chief of staff. "We are proud to be included among the very best in so many specialty areas over such a long period of time."

—John Curtis



ROBERT LISAK

Four of the five members of the Block family in this picture, Daniel Block, Jake Block, Aaron Lewis and Beverly Lewis inherited a mutation in the 10th chromosome that causes a severe form of thyroid cancer. They inherited the mutation from Burton Block, the late husband of Alyce Block, seated.

## A gene mutation passes down generations

Yale surgeon Julie Ann Sosa has performed thyroid surgeries on five members of the same family.

Horizontal scars across their throats, although now fading, remind members of the Block family of what they have been through in the past year. Last summer, doctors at Yale found that this family of cattle farmers from Monroe, Conn., has been passing more than hair and eye color between generations; the family's 10th chromosome harbors a mutation that causes a rare and severe form of thyroid cancer.

Since this discovery, 13 members of the extended family have been diagnosed with the mutation and 10 have had their thyroids removed. Five of the surgeries took place at Yale-New Haven Hospital (YNHH) under the supervision of Julie Ann Sosa, M.D., assistant professor of surgery.

Sosa, who specializes in thyroid cancer, said that the mutation that the Blocks carry, called *MEN2A*, is extremely rare and that most families in this country with the condition have been known to researchers for years. Sosa herself follows five such families. "Many endocrinologists go their whole lives without seeing any cases of this mutation," she said.

But last June, Beverly Block Lewis, 51, learned that she had medullary thyroid cancer. In a very few instances this rare cancer is inherited. "The genetic study we ran came back positive," said Sosa.

Beverly already had hypothyroidism, a deficiency of thyroid hormone, which

she inherited from her mother's side of the family. The condition was the reason for her routine endocrinology appointments. The family assumed the thyroid cancer would also come from the maternal side.

But testing showed that Beverly inherited her mutation from her father, Burton Block, who was then found to have asymptomatic thyroid cancer. Two of Beverly's siblings, her son and two nephews were also diagnosed with the mutation. All but 4-year-old nephew Jake already had cancer.

"Every diagnosis was a new blow," said Alyce Block, Beverly's mother. "Every time was as hard as the first."

For Beverly's recently married son, Aaron Lewis, 28, one of the biggest challenges was thinking about future generations. "Kids that aren't even born yet are going to be affected," he said.

Over the next several months, YNHH became like a second home for the family members, who were constantly in and out of the hospital with each successive surgery.

But every operation went well and the family pulled through. After his thyroid surgery, 83-year-old Burton also survived a near-fatal car accident that landed him back at YNHH, just doors away from where his son Dan was recovering from a pulmonary embolism following thyroid surgery.

In August, more than a year after the family's medical saga began, Burton passed away due to inoperable pancreatic cancer unrelated to the thyroid cancer. "He's really taught us a tremendous amount about strength and patience," said Beverly, standing at Burton's bedside a month before his death. "And the importance of a close-knit family bonding together," added Alyce.

—Sarah C.P. Williams

## Blood vessels made from scaffolds and stem cells soon to be in clinical trials

Two Yale physician-scientists are creating a living organ from scratch, coaxing cells to form artificial tissue that can be used to repair or replace faulty blood vessels. Christopher K. Breuer, M.D., assistant professor of surgery and pediatrics, and Toshiharu Shinoka, M.D., PH.D., associate professor and director of pediatric cardiovascular surgery at Yale-New Haven Children's Hospital, believe their tissue engineering project could lead to the building of more complex organs.

"We figure if you start with blood vessels, that's going to be the first step in making just about anything," said Breuer. "Plus, there's an immediate need for vessels in vascular and cardiovascular surgery."

Because the blood vessels Breuer and Shinoka have created rely on stem cells from a patient's own bone marrow, they are not prone to the inflammation or rejection that affects transplanted tissue. And they are living organs that can grow as a child grows.

When a child is born with such defects as a heart with only a single ventricle, doctors first try to form the child's own tissue into new vessels that can be used as grafts. "But the problem is these children usually require multiple grafts and you never have enough tissue," said Breuer. Such alternatives as synthetic Gore-Tex grafts may lead to infections and blood clotting, while biological grafts from animals tend to calcify and need replacement.

Breuer and his colleagues designed a scaffold in the shape of a vein with

materials used to make absorbable sutures. They then coat the scaffold with bone marrow stem cells. As blood flows through the vein, the stem cells attract cells from elsewhere in the body to form a blood vessel around the scaffolding. As the vessel forms the original matrix dissolves. The resulting vessel can grow over time, and its elasticity matches that of the body's own blood vessels.

Over the past six years, Shinoka has used the process successfully in 47 children in Japan. The technique works well and the grafts have an excellent safety profile, he said, and no patients have needed replacement of tube grafts. Shinoka and Breuer expect to hear soon about their application to the U.S. Food and Drug Administration to conduct clinical trials of their grafts at Yale, but they also continue to pursue improvements in their techniques.

Breuer said that his next goal is to figure out which chemical in bone marrow is attracting cells to the scaffolding. He hopes to isolate that compound and build it into the matrix to eliminate the intermediate step of drawing bone marrow from each patient. "We would have immediate off-the-shelf availability when a patient needed a graft," he said.

—S.C.P.W.

## et cetera ...

### YALE JOINS HYPERTENSION NETWORK

Two School of Medicine scientists will join colleagues in Switzerland, France and Mexico in a collaboration to pinpoint the role of the kidney in high blood pressure. The Transatlantic Network on Hypertension—Renal Salt Handling in the Control of Blood Pressure has received a five-year, \$6 million grant from the Leducq Foundation, a Paris-based organization that supports international research collaborations in cardiovascular disease.

The exact causes of hypertension, one of the most important risk factors for such cardiovascular diseases as stroke and heart attack, remain unknown. The kidney's management of salt levels, however, plays a major role.

Leading the Yale team are Steven C. Hebert, M.D., the C.N.H. Long Professor and chair of cellular and molecular physiology, and Richard P. Lifton, M.D., PH.D., Sterling Professor and chair of genetics.

"The Leducq program," Lifton said, "allows us to bring together a 'dream team' of investigators from around the world with diverse expertise in physiology, genetics and clinical investigation to combine forces to tackle this important medical problem."

—John Curtis

### RESIDENTS FALL SHORT ON STATS

Most medical residents don't understand statistics in medical literature, calling into question their ability to interpret research data, according to a survey by Yale researchers published in the September 5 issue of *JAMA: The Journal of the American Medical Association*. In a survey of 277 internal medicine residents in 11 programs, residents scored an average of 41 percent. Senior residents performed worse than junior residents, suggesting that, with the passage of time, knowledge was lost or not reinforced.

"Most residents in this study lack the knowledge in biostatistics needed to interpret many of the results in published clinical research," said corresponding author Donna M. Windish, M.D., M.P.H., assistant professor of medicine. "Residency programs should include more effective biostatistics training in their curricula to successfully prepare residents for this important lifelong learning skill."

—J.C.

## Rewriting the book on the human genome

After four years of research, an international effort finds that junk DNA may not be junk after all.

A study published in *Nature* last summer has revealed a much more complex view of the vast, uncharted regions of the human genome than previously supposed. “Junk DNA,” noncoding sequences that make up the bulk of the genome’s 3 billion letters, may indeed have a purpose. Now the challenge is to figure out what all that DNA is for. Doing so may prove crucial for understanding complex human diseases.

“We’re trying to map out what’s there,” said Michael Snyder, PH.D., professor of molecular, cellular and developmental biology.

Snyder’s lab is part of the Encyclopedia of DNA Elements (ENCODE) project, a mammoth undertaking of the National Human Genome Research Institute (NHGRI) at the National

Institutes of Health (NIH) involving 35 groups of researchers at 80 institutions in 11 nations. Researchers have spent the last four years sifting through more than 400 million data points to make sense of just 1 percent of the human genome. Their analysis has turned up some surprises.

For one thing, the genome hosts a lot more activity than expected. The conventional wisdom has long held that the important pieces of DNA—the readily decipherable genes making up 1.5 percent of the genome—are converted into RNA via a process called transcription. RNA in turn instructs the cell to make proteins. Scientists have long assumed that in general each gene is transcribed into one RNA fragment and that the remaining gene-free portions of our DNA aren’t transcribed at all.

Not so, according to the ENCODE project. Most letters in the genomic instruction manual wind up being transcribed. Each gene is often transcribed along with a surprisingly large number of nonprotein-coding (NPC) sequences

to produce some extraordinarily long RNA fragments. A single gene can be transcribed into many different RNA fragments of varying lengths. The purpose of all these extra transcripts remains unclear.

Even more perplexing is the prevalence of RNA molecules transcribed entirely from gene-free portions of the genome. NPC RNA transcripts were previously known to exist, but the ENCODE project identified many new ones. Again, their purpose is unknown.

Snyder is even more excited that the project has identified new regulatory regions that do not encode proteins but instead control when, where and to what extent genes are expressed. Recent studies have linked complex diseases with variations in NPC regions of the human genome that could have regulatory functions. Might variations in NPC DNA promote disease by interfering with the expression of genes at distal sites?

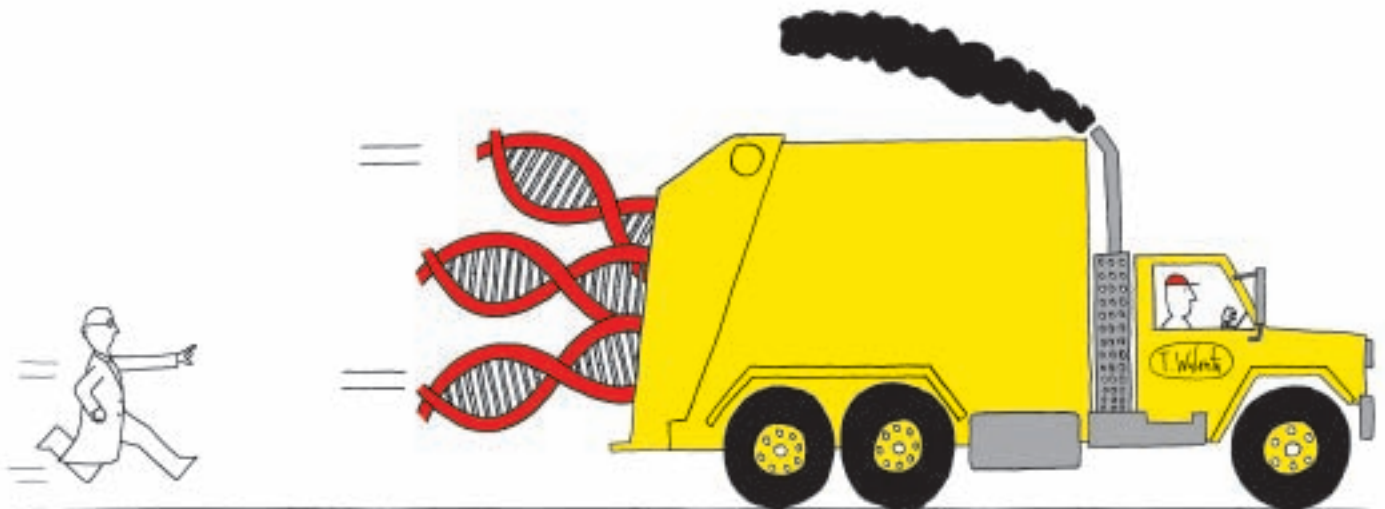
Snyder and his collaborators hope that the project will answer such questions. “This is really what the ENCODE project is all about,” he said.

—Robin Orwant



podcast

A podcast of Michael Snyder speaking on this subject can be found on the Yale page on iTunes U. Visit [itunes.yale.edu](http://itunes.yale.edu) or launch iTunes, then select Yale from the offerings under iTunes U. The podcast is included under “Yale Science.”



## An atomic view of a protein offers insights into a new target for cancer drugs

A research team led by Joseph Schlessinger, PH.D., the William H. Prusoff Professor and chair of pharmacology, has solved the atomic-level structures for active and inactive forms of a protein segment implicated in several types of cancer, opening up a new set of molecular targets for cancer therapies.

The results, reported in the July 27 issue of *Cell*, highlighted previously unidentified changes in the protein's structure that seem to be crucial for its activation. "It gives us totally new avenues for developing drugs for a large group of target proteins that are responsible for several cancers," Schlessinger said.

The study focused on one of 59 receptor tyrosine kinases (RTKs), a set of related proteins whose activities have long been linked with cancer. Normally, RTKs become active only under particular circumstances in order to help cells proliferate, differentiate and survive. But certain mutations in RTKs can turn on the proteins inappropriately, causing aberrant cell proliferation that may lead to cancer. Blocking the activities of RTKs has become a major strategy in anti-cancer drug design.

Two recently developed and highly successful cancer-fighting drugs, Gleevec and Sutent, work in this way. Gleevec is effective against some stomach cancers and leukemias; Sutent works against stomach and some kidney cancers. But Schlessinger, who helped discover Sutent, said many cancers don't respond to Gleevec or

Sutent and those that do develop resistance to the drugs.

Schlessinger's laboratory has spent the last 10 years assembling an atomic-level view of the extracellular domain of an RTK called Kit. By comparing the structure of the protein segment (representing Kit in its inactive state) with that of the active form, his research group has identified changes in Kit that are important in understanding its activation.

The results suggest that in their active state Kit molecules change their shape such that certain portions of the extracellular domain in one Kit molecule move close enough to interact with their counterparts on the other Kit molecule. Schlessinger and colleagues have also provided evidence that these previously unidentified interactions are required for Kit activation, and mutations predicted to strengthen the interactions are known to contribute to various forms of cancer.

Since Kit is part of a family of RTKs with similar extracellular domains, the targets represented by this study probably exist in more than a half-dozen other RTKs that have been implicated in various cancers. "It's a mechanism that is likely to be universal to quite a few of these RTKs," Schlessinger said.

Drugs aimed at these new targets might be effective against Gleevec- and Sutent-resistant cancers, offering hope to many cancer patients who are trying to stay one step ahead of the enemy.

—R.O.

## et cetera ...

### NANOTUBES CAN KILL BACTERIA

A study to measure the toxic effects of nanotubes on human cells has led to a possible new approach to treating antibiotic-resistant infections.

In a paper published in the August 28 issue of the American Chemical Society journal *Langmuir*, Yale researchers said that single-walled carbon nanotubes (SWCNTs) can kill such bacteria as *E. coli*.

"We began the study out of concern for the possible toxicity of nanotubes in aquatic environments and their presence in the food chain," said Menachem Elimelech, PH.D., the Roberto C. Goizueta Professor and chair of chemical engineering. "While nanotubes have great promise for medical and commercial applications, there is little understanding of how they interact with humans and the environment."

Elimelech speculates that the long, thin nanotubes puncture the cells and cause cellular damage. "We are looking at the effects of SWCNTs on a wide range of bacterial strains to better understand the mechanism of cellular damage," Elimelech said.

—John Curtis

### TO BEAT CANCER, EAT YOUR VEGGIES!

Kids aren't the only people who should pile more vegetables on their dinner plate. A study published in the August 1 issue of *JNCI: Journal of the National Cancer Institute* shows that men who regularly eat broccoli, cauliflower, cabbage, Brussels sprouts and turnips are 40 percent less likely to develop advanced prostate cancer than those who consume few of these veggies.

"All these vegetables have compounds called glucosinolates that have been shown to protect cells from DNA damage in the lab, and thus may be anticarcinogenic," said lead author Victoria Kirsh, PH.D., a former doctoral student of Susan T. Mayne, PH.D., professor of epidemiology. Kirsh is now at Cancer Care Ontario.

To make sure that men who consume more vegetables aren't just more likely to get prostate screening tests than others, Kirsh used data that identified 1,338 men diagnosed with prostate cancer out of 29,361 who were screened.

—Sarah C.P. Williams

## Gay men's fears of long-term romance

A psychoanalyst argues that the way gay men's parents treat them affects their adult relationships.

The night in June 1969 that gay men fought police raiding the Stonewall Inn in Greenwich Village marked the beginning of wider acceptance of male homosexuals. Homosexuality has not been considered pathological by mainstream psychiatry since the 1970s, and in the years that followed gay couples have begun to acknowledge their partnerships publicly.

"There's much more social acceptance than there was 20 or 30 years ago," said psychiatrist and psychoanalyst Richard A. Isay, M.D., HS '65.

Many gay men are still suffering, however, said Isay. The main, though not the only, source of their distress, he thinks, lies in the ways their parents treated them as children. He believes that the social acceptance of homosexuality "has not filtered down to the way homosexual boys are raised." Fathers tend to criticize or shun sons who dislike rough sports, play with dolls or otherwise prefer stereotypically feminine pursuits. Mothers who enjoy the sensitivity and shared interests of gay sons may lean too much on them, using them to fulfill their unmet emotional needs.

Isay believes that these dynamics can prevent adult gay men from forming long-term romantic bonds. "Boys may grow up mistrusting the love of another person and will find many other ways of finding the self-esteem enhancement that they missed in childhood," said Isay. Many gay men seek affirmation not through an enduring, loving relationship, he said, but in cultivating large networks of friends, pursuing transient sexual liaisons, focusing on professional success and creating flawlessly appointed environments for themselves.

In his new book, *Commitment and Healing: Gay Men and the Need for Romantic Love*, Isay describes how therapy can help provide gay men with insight into the effects of childhood influences on the capacity to commit to a partner. In a book accessible to nontherapists and illustrated with case



GORDON HARRELL

Richard Isay hopes that his new book, *Commitment and Healing: Gay Men and the Need for Romantic Love*, will lead gay men to examine how their upbringing affects their adult romantic relationships.

studies, Isay shows how gay men can recover from childhood wounds and learn to sustain committed monogamous partnerships. A clinical professor at Weill Medical College of Cornell University and a faculty member at the Columbia University Center for Psychoanalytic Training and Research, Isay draws upon his experience as a Manhattan psychotherapist with mostly gay clients.

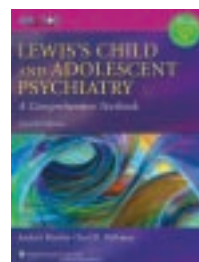
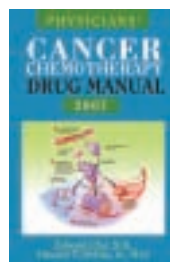
Isay published his first book, *Being Homosexual: Gay Men and Their Development*, in 1989, at a time when he was coming out. He was the first openly gay member of the American Psychoanalytic Association. His 1996 book, *Becoming Gay*, outlines the ways in which gay teenagers and adults develop self-acceptance.

Isay said that his new book has stirred up some controversy because he argues that gay couples who tolerate sexual adventures outside the partnership may do so out of an unconscious fear of closeness rather than a sense of liberation from traditional heterosexual strictures. "It runs counter to the prevailing doctrines of the gay community that maintain that our relationships are fine, more democratic and better than heterosexual relationships," said Isay.

He hopes that his new book will help gay men to examine the patterns of their romantic relationships and perhaps seek the guidance of a therapist attuned to gay issues. He'd like parents to pay attention to the way they treat their sons. Ideally, he said, even when a son doesn't act like a typical boy, "if both father and mother love him as they do their other children, if they value what he has to say about his attractions to others, then they can inculcate the value of love and can greatly influence how he forms loving relationships as an adult."

—Cathy Shufro

*Bookshelf* focuses on books and authors at the School of Medicine. Send suggestions to Cathy Shufro at [cathy.shufro@yale.edu](mailto:cathy.shufro@yale.edu).



### **Brain Tumors: Practical Guide to Diagnosis and Treatment**

by Joseph M. Piepmeyer, M.D., HS '82, the Nixdorff-German Professor of Neurosurgery, and Joachim M. Baehring, M.D., assistant professor of neurology and neurosurgery (Informa Healthcare) This reference provides information to help clinicians make accurate diagnoses and select the most appropriate treatment regimens for patients with primary and metastatic brain tumors or neurological complications of cancer. The guide reviews the epidemiology, identification and management of brain tumors while explaining the latest advances in the field.

### **Management of High-Risk Pregnancy: An Evidence-Based Approach, 5th ed.**

by Catherine Y. Spong, M.D., John Queenan, M.D., and Charles J. Lockwood, M.D., the Anita O'Keefe Young Professor of Women's Health and Obstetrics, Gynecology and Reproductive Sciences (Blackwell Publishing) This fifth edition focuses on factors affecting pregnancy, including genetics; diagnostic techniques; maternal diseases; biochemical and biophysical monitoring; anesthesia; complications of labor and delivery; and neonatal considerations. A resource for perinatal care and a reference guide to diagnosis and management of high-risk pregnancies, the book takes an evidence-based approach and expands on several important areas: genetics, Doppler ultrasound, AIDS, Group B streptococcal infections, pre-eclampsia and prematurity.

### **Physicians' Cancer Chemotherapy Drug Manual, 2007**

by Edward Chu, M.D., professor of medicine (medical oncology) and pharmacology, and Vincent T. DeVita Jr., M.D., HS '66, the Amy and Joseph Perella Professor of Medicine (medical oncology) and professor of epidemiology (Jones and Bartlett Publishers) Completely revised for 2007, this handbook provides an overview of the field of cancer chemotherapy. It includes a comprehensive catalog of more than 100 drugs commonly used in cancer treatment, including several new agents. The authors discuss antiemetic drugs; clinical pharmacology; indications and dosages; and toxicity and drug interactions. The book also provides diagrams of drug structures and metabolic pathways.

### **Soft-Tissue Surgery of the Craniofacial Region**

by John A. Persing, M.D., professor of surgery (plastic) and neurosurgery; and Gregory R.D. Evans, M.D. (Informa Healthcare) This reference work covers the latest technologies in soft-tissue surgery to improve function and enhance cosmetic appearance for patients with disfiguring and debilitating facial defects from trauma, congenital deformity or disease. The book includes chapters on laser imaging, burn treatment, cleft palate reconstruction and facial paralysis.

### **Lewis' Child and Adolescent Psychiatry: A Comprehensive Textbook, 4th ed.**

by Andrés S. Martin, M.D., M.P.H., associate professor in the Child Study Center and of psychiatry, Fred R. Volkmar, M.D., the Irving B. Harris Professor in the Child Study Center and professor of psychiatry, pediatrics and psychology, and the late Melvin Lewis, M.B.B.S., HS '59, former professor emeritus and senior research scientist in the Child Study Center (Lippincott, Williams & Wilkins) The fourth edition of this classic text emphasizes the relationship between basic science and clinical research and integrates scientific principles with the realities of drug interactions. The book has been thoroughly updated, with two-thirds of the contributions coming from new authors. It also combines discussions of economic factors and diversity in the patient population with a strong focus on evidence-based practice. New chapters consider genetics; research methodologies and statistics; and the continuum of care. A companion website provides searchable access to the text.

### **Manual of Dermatologic Therapeutics: With Essentials of Diagnosis, 7th ed.**

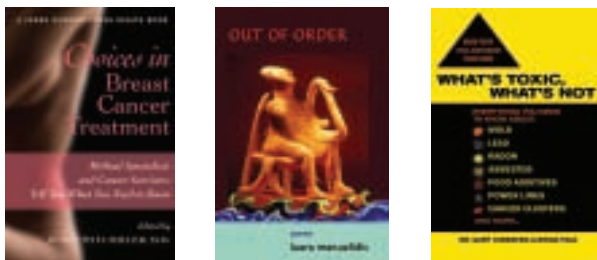
by Kenneth A. Arndt, M.D. '61, HS '62, and Jeffery H.S. Hsu, M.D. (Lippincott, Williams & Wilkins) This manual outlines the pathophysiology, symptoms, clinical findings and assessment of skin diseases as well as offering detailed guidelines for choosing among therapeutic options. An up-to-date formulary provides information on medications and other products used in dermatology.

### **Cell Biology: With STUDENT CONSULT Online Access, 2nd ed.**

by Thomas D. Pollard, M.D., Sterling Professor of Molecular, Cellular and Developmental Biology and professor of molecular biophysics and biochemistry and of cell biology, William C. Earnshaw, Ph.D., and Jennifer Lippincott-Schwartz, Ph.D. (Saunders) This text offers a modern approach to the study of cell biology. It explores the ways in which cellular structure, function and dysfunction result from specific macromolecular interactions. Boxes on most pages contain key principles, helpful summary tables, diagrams and research figures. The second edition contains a new chapter on the origin and evolution of life.

### **Preventive Cardiology: Insights Into the Prevention and Treatment of Cardiovascular Disease**

edited by JoAnne Micale Foody, M.D., associate professor of medicine (cardiology) (Humana Press) This new three-part edition provides an overview of opportunities to prevent the progression or, in some instances, reverse the process of coronary atherosclerosis and incorporate these strategies into the daily practice of clinical medicine. It represents a move away from the emphasis in the 1990s on technological interventions toward a molecular perspective. This book provides clinical cardiologists, internists, primary care providers and allied health care professionals with the tools and understanding necessary for practicing preventive cardiology.



### Pocket Guide to Chemotherapy Protocols, 4th ed.

by Edward Chu, M.D., professor of medicine (medical oncology) and pharmacology (Jones & Bartlett Publishers) Spiral-bound and arranged alphabetically by cancer type for easy access, this pocket guide serves as a quick reference for physicians, nurses and other health care providers treating cancer patients. The guide contains combination and selected single-agent regimens for solid tumors and hematologic malignancies. The regimens selected are based on published literature and are used in clinical practice in the medical oncology community.

### Choices in Breast Cancer Treatment: Medical Specialists and Cancer Survivors Tell You What You Need to Know

edited by Kenneth D. Miller, M.D., assistant professor of medicine (medical oncology) (Johns Hopkins University Press) This book combines contributions from specialists with personal narratives by breast cancer survivors. Topics covered include risk factors, screening, genetic testing, prevention, diagnostic methods, the doctor-patient relationship, surgical treatments, adjuvant treatments, breast reconstruction and clinical trials.

### Out of Order: Poems

by Laura M. Manuelidis, M.D. '67, HS '70, professor of surgery (neuropathology) (iUniverse) Although she is best known

for her work on spongiform encephalopathies, Manuelidis is also a poet whose work has appeared in the *Nation* and the *Connecticut Review*. In this collection, she writes of love and loss, of places remembered and of life's wonder and pain.

### What's Toxic, What's Not

by Gary L. Ginsberg, Ph.D., lecturer in epidemiology, and Brian Toal (Berkley Trade) Every day, people work, live and play amid potentially harmful toxic substances, sometimes unwittingly. People are exposed to these substances in their homes, neighborhoods, schools, workplaces, foods and other consumer products. This comprehensive guide distinguishes between risks and myths, explaining how to identify problems and what to do about them. Charts to help assess risk, a special homebuyer's guide and Q&A segments discuss mold, lead, radon, asbestos, food additives, power lines, arsenic, mercury, pesticides, dioxin and toxic gases, as well as ways to guard against them.

*The descriptions above are based on information from the publishers.*

SEND NOTICES OF NEW BOOKS TO Cheryl Violante, *Yale Medicine*, 300 George Street, Suite 773, New Haven, CT 06511, or via e-mail to [cheryl.violante@yale.edu](mailto:cheryl.violante@yale.edu)

## For the busy researcher, help from medical librarians with publishing papers

Picture the typical researcher's desk, with journals piled high. Now imagine a librarian who can make those journals disappear—and reappear in a customized electronic library.

Perhaps you're an investigator ready to submit an article. After countless revisions you need a fresh pair of eyes. Enter an editor, referred to you by the medical library. The editor checks for spelling, punctuation and grammar and suggests ways to streamline the piece. And here comes a librarian who will walk you through the software that will format your citations and bibliography to conform to the journal's style.

Your article has been accepted—and published! You know you should submit it to PubMed Central, the free online archive of biomedical and life science journals operated by the NIH's National Center for Biotechnology Information in the National Library of Medicine. But you're busy. And you've spent enough time on that article. No problem: a librarian from the medical library will submit it for you.

These are a few of the services provided by librarians at the Cushing/Whitney Medical Library—the new Publishing Support page on the library website describes all that they do.

Services include classes on using the library, links to online style manuals and help choosing bibliographic software. The Publishing Support page lists liaison librarians, who are specialists assigned to each department and research center to provide guidance to researchers in their area.

Other support services include information on a given journal's impact factor, which is based on how often articles are cited in journals. Other information on the support site includes instructions for formatting papers; information on copyright issues; lists of library classes; and online tutorials on topics including scholarly publishing and using Ovid MEDLINE.

The new page, said Reference Librarian Lynn H. Sette, M.L.S., "is a natural extension of the kinds of things we have always done for people. Publishing and the library go hand in hand."

The page can be accessed from the Cushing/Whitney home page or at <http://www.med.yale.edu/library/publishing.html>.

—Cathy Shufro

*In Circulation* focuses on activities at the Cushing/Whitney Medical Library. Send suggestions to Cathy Shufro at [cathy.shufro@yale.edu](mailto:cathy.shufro@yale.edu).



**ROBERT FINE****A third party to speak for the terminally ill**

Doctors and nurses in cases involving medically futile treatment often clash with a patient's loved ones over whether to continue that treatment. An extrajudicial process, however, allows both sides to appeal to a committee of physicians, nurses, community representatives and other caregivers, a medical ethicist told an audience at pediatric grand rounds in September.

The Texas Advanced Directives Act of 1999, the first statewide attempt to resolve such disputes, has created "a legal safe harbor," said Robert L. Fine, M.D., director of the Office of Clinical Ethics at Baylor Health Care System. When a case is deemed futile, it may go before the ethics committee, which does not always agree with the medical team. If the committee agrees with the medical team, treatment may be withdrawn unless an alternative health care provider is found within 10 days.

Most cases are settled within the 10-day process. "In many cases the family is relieved," said Fine, who helped write the Texas law. "They didn't let go. It lifted the burden." Doctors are relieved, too. "Sometimes the highest level of care is to withdraw medically inappropriate treatment."

—John Dillon

**GERALD FRIEDLAND****TB, an Atlanta lawyer and 52 South African patients**

At first glance a diagnosis of tuberculosis seems to be all that unites Andrew Speaker, an Atlanta lawyer, with 52 impoverished South Africans who died of drug-resistant TB in a remote rural area in 2005. The cases "couldn't appear more different on the surface," said Gerald Friedland, M.D., professor of medicine and epidemiology at Yale, at internal medicine grand rounds in August.

Speaker made headlines last spring after being diagnosed with extensively drug-resistant tuberculosis (XDR-TB) and then putting fellow airline passengers at risk by traveling on seven separate commercial flights. He later received treatment at a top-rated TB hospital. Most of the rural South Africans, on the other hand, had all died by the time laboratory testing revealed the diagnosis of XDR-TB, said Friedland, who reported the cases in *The Lancet* in 2006.

Friedland said both Speaker and the South Africans suffered from the slowness of TB diagnostic tests and limited treatment options for drug-resistant TB. Friedland says the presence of growing numbers of cases with XDR-TB underlines the longstanding neglect of TB and the more recent rise of TB and HIV coinfection. "If there's a silver lining," he said, "it's that the world attention focused on both of these cases has been a wake-up call for the need for resources to promote scientific advances and improved care for TB."

—Cathy Shufro

**JAMES MONGAN****Seeking a national solution to health care for all**

Medicine is witnessing the best and worst of times because of the "staggering difference" between lifesaving advances and the "very broken" economics of health care delivery, said James J. Mongan, M.D., president and CEO of Boston-based Partners Health-Care System, during a talk at the medical school in September.

Mongan, who delivered the 11th annual Samuel O. Thier Lecture in Health Policy, said that the landscape of health care finance has shifted from one dominated by government programs to a regulatory/free-market hybrid that includes Medicare, Medicaid and managed care. Attempts to broaden coverage through employer mandates have failed because of a "tenacious desire for autonomy" in the private sector—businesses have exploited "our national ambivalence about heavy-handed government regulations" and taxation.

Meanwhile, 45 million uninsured Americans get emergency room treatment when they are sick instead of preventive care. Ignoring the cost of this tendency is dangerous, Mongan warned. While Massachusetts has a "promising" if flawed system to insure its residents, providing health care for all citizens "will demand some national action," Mongan said, though he wasn't optimistic that such action could be taken in the heat of a presidential campaign. "We currently stand as a nation without a good answer."

—J.D.

**ANDREW VON ESCHENBACH****Speeding the pace of biomarker discovery**

Biomarkers that identify cancer in its early and more treatable stages have emerged as the newest tools in its prevention, diagnosis and treatment. But according to Andrew C. von Eschenbach, M.D., commissioner of the Food and Drug Administration (FDA), a urologic surgeon and oncologist as well as a cancer survivor himself, more effective collaboration among scientists and between the public and private sectors is needed to hasten the discovery of these molecular or cellular indicators of disease states.

"We have enormous talent but we haven't brought it together," von Eschenbach said in October at "Discovery to Delivery: A Public Forum About the Future of Cancer Research," a colloquium sponsored by Yale Cancer Center, Yale-New Haven Hospital and Friends of Cancer Research. "We have superstars, but not a superstar team."

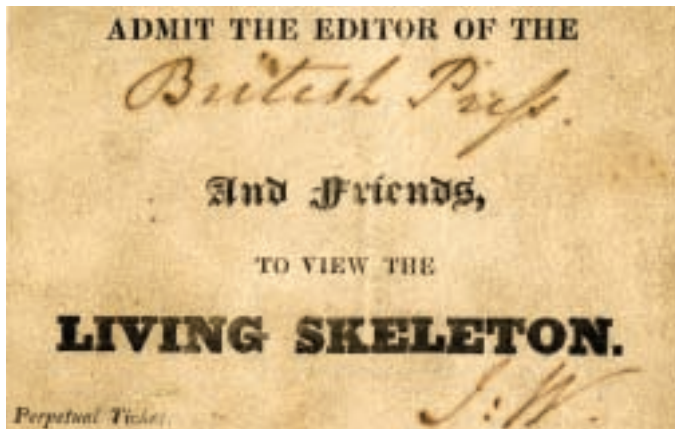
To bring researchers together, the FDA has joined the Foundation for the National Institutes of Health, the National Institutes of Health and the Pharmaceutical Research and Manufacturers of America to launch the Biomarkers Consortium. This public-private biomedical research partnership will make its findings on newly discovered biomarkers available to scientists worldwide.

—Jennifer Kaylin

## Preserving a rich trove of texts and artifacts

A preservation librarian conserves and preserves books and objects from medicine's earliest days.

By Cathy Shufro



THE HARVEY CUSHING/JOHN HAY WHITNEY MEDICAL LIBRARY (3)



**CLOCKWISE FROM ABOVE LEFT** Claude Seurat, whose physique was excessively bony, was exhibited at freak shows as the Living Skeleton in London in 1825.

*Figure of a pregnant woman*, a woodcut with hand color, is from *Fasciculus Medicinae*, one of the first printed medical books with anatomical illustrations. This collection of medical treatises was published in Venice in 1491.

*A lesson in dissection*, also a woodcut with hand color, comes from *Fascicolo di Medicina*, a 1493 Italian translation of *Fasciculus Medicinae* from the original Latin.

The *Catoptrum Microcosmicum* resembles a child's flap book, in which you lift a flap showing a beach ball to discover a kitten. But this book, nearly 400 years old, is a multilayered map of the human body. Raise the skull flap to see the brain beneath the bone. Turn aside the belly flap to reveal the intestines. Some pages have up to 15 layers of anatomical structures—detailed engravings made from copper plates.

This 1613 version of the rare and precious anatomy text by German physician Johann Remmelin is among the treasures in the locked stacks of the Medical Historical Library. The collection includes handwritten manuscripts, among them the *Paneth Codex*, an early 14th-century compendium of texts. The codex includes works by Hippocrates, Galen and Avicenna. Also in the collection are 325 medical incunabula, materials produced during the infancy of printing from 1450 to 1500.

Items in the collection range from antique gynecologic instruments to 19th-century stereoscopic slides of skin ailments, with a viewer for seeing them in 3D. The collection also includes scores of public health posters in Farsi, Chinese and various Indian languages; 2,000 photographs, from daguerreotypes to modern digital images; and the Fry Collection of prints and drawings of medical and health-related subjects across five centuries.

The world-renowned historical collection comprises 130,000 books, bound manuscripts and pamphlets, along with several thousand medical and scientific instruments and weights and measures. “The Historical Library houses one of the world’s finest historical medical collections, and because of its wide variety of objects, poses large challenges to preservation,” said preservation librarian Sarah A. Burge, M.L.S.

Burge, hired as the first preservation librarian for the Cushing/Whitney Library in 2005, has begun a full preservation program for the collection. She devotes her time to the historic materials, which attract scholars from all over the world. Many of the rare books came from the collections of surgeon Harvey W. Cushing, M.D., physiologist John F. Fulton, M.D., and tuberculosis specialist Arnold C. Klebs, M.D.—all bibliophiles—whose donations formed the backbone of the historical library founded in 1941. “They had a real appreciation of the book as an object and the book as content,” said Burge.

Some of Burge’s challenges are technical. For instance, because the health of the books depends on the right environmental conditions, Burge is working with the medical school’s heating and ventilation experts. Their dream: air temperature at 65 degrees Fahrenheit, humidity at 40 percent, no fluctuations. Other challenges are more abstract: Burge has helped draft policies to allow students and

scholars to use the collection while protecting it from damage or the kind of theft that occurred at Yale’s Beinecke Rare Book and Manuscript Library in 2005, when dealer E. Forbes Smiley III stole several rare maps from the collection.

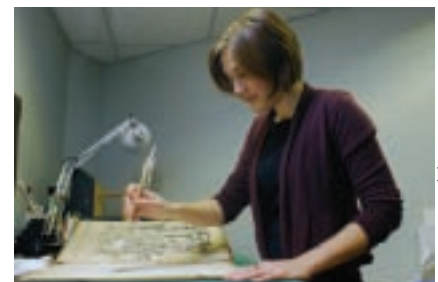
Paradoxically, many of Burge’s challenges result from the rise of literacy in the 1830s, when advances in papermaking put books in the hands of ordinary people. New steam-powered machines and a scarcity of linen transformed the paper industry. For the first time, paper was made primarily from wood pulp rather than cotton or linen fibers. And wood-pulp paper doesn’t last; it becomes brittle as a result of acid decay through a process known as slow fire.

“The brittle-book problem is what I’m fighting with our 19th-century materials,” said Burge, who studied book preservation at the University of Illinois at Urbana-Champaign. Embrittlement can be halted by a process called deacidification, while books too fragile for public use can be digitized or microfilmed. “The historical library’s long-standing mission includes the understanding that library materials will be used, and with use comes wear and tear,” said Burge. “Our goal is to keep our collections safe and in useable condition through preservation and conservation measures.”

Cathy Shufro is a contributing editor of *Yale Medicine*.

**RIGHT** Among the tasks facing preservation librarian Sarah Burge is preserving books made of wood pulp that becomes brittle with age. She triages the books according to damage, value and their importance to the collection.

**FAR RIGHT** Burge uses a powder made of crumbled rubber erasers to clean the surfaces of the pages of *Catoptrum Microcosmicum*, a 400-year-old anatomy text.



JOHN CURTIS (2)

# On the wards in Uganda

Story and Photographs  
by John Curtis

For Yale physicians and medical students, a few weeks at Mulago Hospital in Kampala become a life-changing experience.



In the infectious disease ward at Mulago Hospital in the Ugandan capital of Kampala, a woman in her early 20s lies on a bed with only a thin sheet to ward off the morning chill. Alone, suffering from complications from AIDS, her few possessions in a cardboard box at her bedside, she has no family to bathe her, bring her food or give her medicine. These are what doctors here call poor “blanket signs.” The mere presence—or absence—of a blanket speaks volumes.

Even before they measure the blanket signs, however, the doctors know several things about their patients. They know that as a national government-run referral hospital, Mulago receives the sickest of the sick. They know that more than half the patients in the hospital are infected with HIV. They know that two-thirds of their patients will die in the hospital or within two months of leaving it. And they know that most of their patients are too poor to afford more than the most basic tests and treatments.

Blanket signs will tell them more. The hospital provides patients with a bed. Patients must bring sheets, blankets and pillows, as well as “attendants”—family members who care for them. The doctors have learned that just having a blanket reveals much about a patient’s economic status. Of necessity, the patient’s ability to pay will drive the treatment regimen. If the patient has no resources, the doctors will prescribe only the drugs that come free from the pharmacy and order only the tests that the hospital provides at no cost.

“Medicine is not all about what you have learned in medical school,” said Robert Kalyesubula, M.D., a Mulago resident. “You prioritize. In the context of the limitations you have, what can you best do for this person? What is going to help my diagnosis best? You talk to them so they find a way to get the money, sacrifice a few things. You save the most expensive tests for last, when you really need them.”

### Making an impact on the globe

Improving patient care in New Haven as well as in Kampala is the goal of a collaboration that began in August 2006, when Majid Sadigh, M.D., associate professor of medicine, arrived at Mulago with a team of Yale residents. Since then Yale has maintained a constant presence at the hospital, with Yale residents and attendings in monthlong rotations alongside colleagues from the Faculty of Medicine at Makerere University and Uganda’s Ministry of Health. In the summer of 2007 Yale expanded its presence to include three medical students on new international fellowships (See sidebar, p. 29); a physician from Russia; two Downs Fellows; two public health students pursuing research projects; and students from the Physician Associate Program in addition to three Yale residents.

The collaboration grew out of Sadigh’s visit to Uganda in 2002 to lecture and teach about infectious disease. Why, he wondered, was the extraordinary clinical, medical and epidemiological research taking place at Makerere not finding its way literally across the street to improve care at Mulago Hospital? Yale, he felt, could help. “It is one of the best universities in the world,” he says. “It has a vision of having an impact on the globe. It has the most talented individuals.”

In the face of despair and crushing poverty Sadigh has implemented several ideas, large and small, that have made things better for people in Uganda. In the fishing village of Kasensero, the home of the earliest-known AIDS case in Uganda, Sadigh has helped patients at the local clinic and raised money to provide an education for orphans. At the nearby Holy Family Nazareth School, a boarding high school where most of the 250 students have been orphaned by AIDS, he has raised money for bunk beds and solar panels to provide lighting. And at Mulago he has kept the exchange going for more than a year with support from Yale’s Department of Internal Medicine and the Yale/Johnson & Johnson Physician Scholars in International Health program, which funds residents’ trips to Mulago.

When Sadigh first contemplated the collaboration in 2002, he and Asghar Rastegar, M.D., vice chair of medicine, had already launched a successful program between Yale and the state medical school in Kazan, Russia. Residents from both countries have traveled back and forth for clinical rotations for several years. With support from Rastegar and

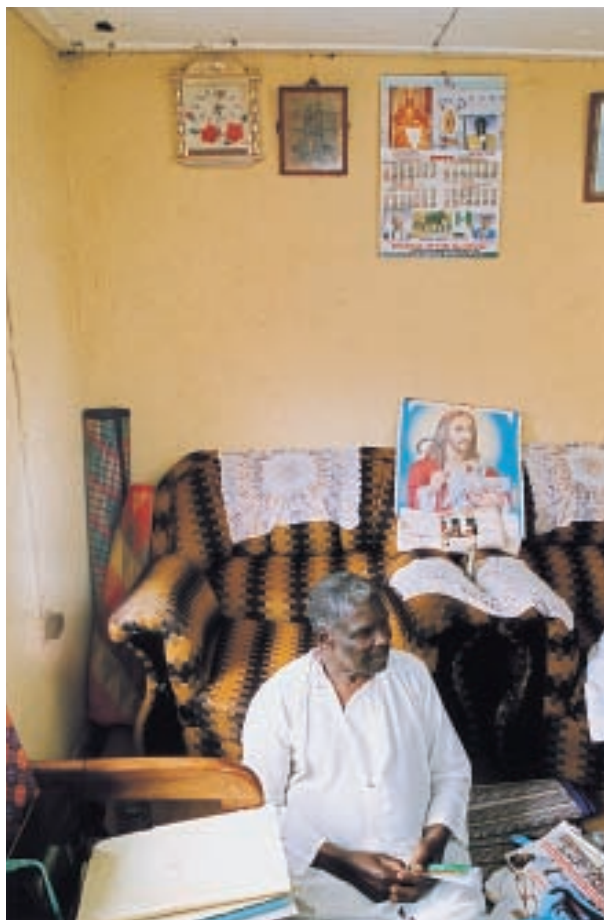
**PREVIOUS PAGE** With an attendant nearby and blankets, sheets and a pillow on her bed, this patient had what doctors at Mulago Hospital call good “blanket signs.” What the patients bring with them gives doctors clues to their financial resources and helps doctors tailor their treatment plans.



On the cardiology ward, José Evangelista, a third-year Yale resident, rounded with Caroline Bwango, a resident, and Simon Eleku, a medical registrar, or junior faculty, at Mulago Hospital last summer. Evangelista returned to New Haven with a stronger appreciation of the physical exam. “Before jumping to a test I go back to the physical exam to see if I missed anything,” he said. “I don’t order labs nearly as much as I used to unless there is a rationale.”



In a laboratory at Mulago Hospital, technician Samson Omgot showed the Yale residents how to test for malaria in a blood sample. Throughout their time in Uganda, the residents saw diseases or stages of disease that are rare in the United States. “They are extremely good at what they do,” said Yale resident Mike Lee, left, describing his Ugandan colleagues. “They can show us so many things in working with limited resources. Their knowledge of tropical medicine is amazing.”



This patient, a 75-year-old mechanic with diabetes and hypertension, kept a notebook detailing his medical condition over the previous 10 years. “He needs more insulin,” said Peter Ellis, an attending at Yale-New Haven Hospital, after looking over his records. “His sugars are too high.” Ellis suggested a higher dose of insulin at lunch to cover the heaviest meal of the day.

David L. Coleman, M.D., HS '80, interim chair of internal medicine, Sadigh laid the groundwork for the Uganda exchange. By the summer of 2006 both sides had signed a memorandum of understanding.

Both Yale and Makerere, they believed, could benefit from an exchange that would not, in the words of Rastegar, be an exercise in “medical tourism.” Yale doctors would learn more about tropical and infectious diseases, while Ugandan doctors would gain access to the latest medical standards and methods.

In practice, however, the lessons that Yale students, residents and attendings learn from their Ugandan colleagues go much deeper than improving clinical skills and acquiring knowledge. The Mulago rotations bring into question basic notions about medicine and the very concept of what it means to be a doctor. This soul-searching begins on the first encounter with the wards at Mulago.

At the 1,500-bed hospital Yale physicians have few of the tools they take for granted in the United States. Patients in Mulago are often in a hospital for the first time in their lives and little or no medical history is available. They arrive in an advanced stage of disease. The hospital pharmacy may have run out of basic medications. No one is available to take a patient downstairs for an X-ray. Test results may take days to arrive. One Yale student took to carrying a blood pressure cuff with her on rounds since none was available. During a teaching session the students wandered the wards in search of a working light box so they could look at X-rays. And it's not always clear who's in charge of a patient, making sure that tests are done and medications are administered.

“When people come here they can really feel bewildered,” says Sam Luboga, M.D., deputy dean of the Faculty of Medicine at Makerere University. “They find a hospital full of patients without drugs, without supplies.”

That brings them to a new appreciation of the basic skills of medicine, says Christophe K. Opio, M.D., an internist at Mulago. “You have to make a diagnosis from the little information you have,” he says. “You become an investigator. You use all of your senses to identify a problem and then know what to do about a problem.”

From their Mulago colleagues Yale doctors learn to rely on the most basic tools of medicine—a rigorous physical examination, whatever history can be gleaned from the patient and their own knowledge of disease. And that is





During their stay in Uganda, Yale attendings and students went on house calls on the outskirts of Kampala. Traveling with a team from St. Stephen's Hospital, a private facility in the suburb of Mpererwe, they made follow-up visits to patients. The hospital treats about 10,000 patients a year from a catchment area that includes Mpererwe and adjoining neighborhoods. Malaria accounts for more than a third of the cases at the small hospital, which operates on fees and with support from charities in the United Kingdom. Sam Luboga, the deputy dean at Makerere University's Faculty of Medicine, started the hospital about 20

years ago. Hospital administrator Charles Mugume explained the importance of the house calls. "They come, we treat, we discharge. Then we follow up," he said.

Majid Sadigh led house calls in July, accompanied by his son, Kaveh, a medical student at Tulane, and Matt Cook, who graduated in October from Yale's Physician Associate Program. The team from St. Stephen's Hospital included the hospital administrator, a midwife, a social worker and an attendant. The catchment area is not a suburb like any in the United States. Few roads are paved and the houses, often of brick or cinder block, are surrounded

by plantain trees or small pastures for grazing goats or cows.

**TOP LEFT** Sadigh tended to an 85-year-old woman with multiple problems, including hypertension and cataracts that could lead to glaucoma.

**BOTTOM LEFT** Charles Mugume, administrator of St. Stephen's Hospital, took a patient's blood pressure.

**TOP RIGHT** Peter Ellis led house calls with medical students Allison Arwady and Lily Horng. Their day started with rounds at the hospital, where they were served a typical Ugandan lunch of rice,

*matoke* (mashed plantain) and stew. At the home of a 75-year-old mechanic, Ellis reviewed the patient's medications.

**BOTTOM RIGHT** House calls often involved a search for the patient's home. Medical student Allison Arwady struck up a conversation with a patient's relative during one search.



Mulago resident Robert Kalyesubula, 31, comes from Luwero, a town about 60 kilometers north of Kampala, where he spent part of his residency. “When I practiced in my hometown I realized that there were so many patients so far from doctors,” he said. His experiences during the civil war that followed the overthrow of Idi Amin led to his decision to help people by becoming a doctor. His father died in the fighting and Kalyesubula was separated from his mother. He also lost siblings to war, disease and starvation. Sponsored by a Canadian charity, Friends in the West, he was

raised in an orphanage and as a child toured the United States as a member of the African Children’s Choir. Later he went to McMaster University in Canada as part of a medical exchange. “There is a lot to learn between the two of us,” he said of the Makerere-Yale collaboration. “We know a lot about infectious diseases. They know a lot of modern medicine. We exchange at that level.” His main lesson for Yale medical students was, “how you can actually manage patients by having a very good clinical exam.”

the main lesson. “You’re not a doctor if you can only function in a certain milieu,” Sadigh says. “Sometimes there’s just you and the patient.”

### The Harvard of East Africa

Any discussion of health care problems in Uganda starts and ends with money. Uganda is a poor country; annual per capita income is about \$280. Foreign aid accounts for half the national budget revenues. The country has dismal health indicators—life expectancy, 52 years; infant mortality, 67 per 1,000 live births. The risk of bacterial diarrhea, hepatitis A, malaria and African sleeping sickness is very high.

And the country is still recovering from the turmoil that followed independence from Great Britain in 1962. Nine years later, when General Idi Amin seized power in a coup, Ugandans welcomed him as a relief from the autocratic President Milton Obote. Within a year Amin began to expel the country’s Asian population—brought to Africa as civil servants by the British—who, Ugandans felt, unfairly dominated the economy. The Asians also made up a significant portion of the medical school faculty.

“I had just started medical school when Amin came to power,” said Nelson Sewankambo, M.D. He is the sixth Ugandan dean of the Faculty of Medicine, a post he has held for almost a decade. “We saw the exodus of expatriate staff at the time. Ugandans and Africans also left.”

As Amin targeted his enemies, real and perceived, Sewankambo said, academics “became suspect.” Several doctors at the medical school were murdered, including one who was snatched from the operating room. By 1979, when neighboring Tanzania invaded Uganda over a border dispute and Amin fled to exile in Saudi Arabia, Mulago Hospital had no working X-ray machines, no running water, no refrigeration in the morgue and no sewage system. The General Medical Council of the United Kingdom no longer recognized Makerere medical degrees.

This loss of recognition was a stunning reversal for both the medical school and the university that had been known as the Harvard of East Africa. Makerere University opened in 1922 as a technical school. Over the next few years it added courses in agriculture, veterinary medicine and teacher training. In 1924 the precursor to the medical school, the School for Senior Native Medical Assistants, opened at Mulago Government Hospital. Even the school’s

name reflected the colonial view that Africans were incapable of becoming doctors. By 1929, however, the school for medical assistants had become the Faculty of Medicine, graduating not assistants but fully qualified physicians. The university advanced in other areas after it affiliated with the University of London in 1949. By 1962 Makerere was East Africa's leading educational institution, producing several presidents of new African nations, including Julius Nyerere of Tanzania. In 1963, following Uganda's independence, Makerere joined with universities in neighboring Kenya and Tanzania to form the short-lived University of East Africa.

Makerere, like the rest of the country, fell on hard times during the Amin era and the civil war that followed. Fighting ended in 1986, when Yoweri Museveni's guerrilla band took power. Museveni has ruled ever since, providing stability in Uganda if not true democracy or transparency.

As peace came to the country Makerere University sought to regain its former prestige. An opportunity emerged for the Faculty of Medicine in the early 1980s on the shores of Lake Victoria, where a mysterious ailment was plaguing the fishing village of Kasensero, about 60 miles southwest of Kampala.

In 1982 people in the village began dying of a disease the locals called "slim" because of its wasting effect. The disease was AIDS but no one knows how it reached the village. HIV had made the leap from monkeys to humans years earlier in Cameroon on Africa's western coast. Some speculate that the AIDS virus crossed the continent with the construction of a trans-Africa highway. Others blame its arrival in Uganda on the invading Tanzanian army. However the virus arrived, it turned this village and its brothels into the epicenter of the Ugandan AIDS epidemic. Since then much of the leading research on AIDS in Africa has been done at Makerere.

"From the beginning the medical school has been the flagship of Makerere University. There is good research on HIV. There is groundbreaking research on malaria as well. Burkitt's lymphoma was described by a professor here," said Sewankambo, a prominent AIDS researcher. Yet problems persist. "Makerere continues to struggle in raising resources. ... The salaries are awful, for example. Laboratories are run-down. The equipment is old."

The medical faculty at Makerere has long enjoyed help from abroad. Before implementing a new problem-based cur-

riculum in medicine, faculty members visited 14 universities around the world. And international collaborations don't end there. Makerere's medical school has many foreign partners—Case Western Reserve University; Johns Hopkins University; the University of California, San Francisco; the University of Medicine and Dentistry of New Jersey; McMaster University in Canada; the University of British Columbia; the University of Dublin; and the University of London. The Yale-Makerere collaboration, however, stands apart.

"Other universities say, 'Let's collaborate on research.' Yale is interested in improving the quality of health care services and the education of physicians," says Sewankambo. "By improving education we are training health workers to provide quality services within the context of limited resources."

#### **"That is how we survive."**

In resource-poor Mulago Hospital, the Yale residents and students rotating through the wards last summer incurred a debt to their Ugandan hosts that they doubted they could repay. As they worked side by side with Ugandan colleagues their physical examination skills soared; they learned about tropical diseases; and they saw what were for them uncommon cases of advanced disease. The three medical students agreed that Mulago provided their best clinical rotation by far. But they all wondered how much they were helping Mulago Hospital in return. How could they repay the hospital for all that they were learning? If Yale residents and even attendings struggle in the absence of resources that are second nature to them, what can they teach physicians who lack those resources?

"You can always help, even when the facilities are not as good as where you are from," says Edward Ddumba, M.D., executive director of Mulago Hospital. Echoing Sadigh, he adds, "You cannot be paralyzed by different institutions. People adapt."

Ddumba has no trouble imagining where he'd spend more money if he had it. He'd like to double the number of physicians on staff from 400 to 800 and increase the nursing staff as well. Among his other goals are "to get the infrastructure repaired ... to get hospital furniture, hospital linens, improve laboratory services, improve emergency drug supplies and emergency response infrastructure using capital budget."

Most of his \$15.6 million annual budget comes from the Ugandan government. Private wards on the sixth floor

generate additional income and the hospital also relies on international donations of supplies, money and drugs. “That is how we survive,” Ddumba says.

Sadigh believes Yale doctors also provide a significant contribution to the hospital. In the first year of the program, said Sadigh, Yale residents provided 90 weeks of coverage at the hospital and attendings provided 60 weeks. They set an example by modeling different attitudes and ways of practicing medicine and interacting with patients. “If we have any impact on Mulago, we have an impact on the whole country,” Sadigh says, “because Mulago is setting the standard for care and education for the country.”

Among the tangible benefits are the medical supplies that Yale visitors bring from Recovered Medical Equipment for the Developing World (REMEDY), a Yale-based organization that salvages surgical supplies and other unused materials that can’t be used in the United States. The visitors also bring journals and textbooks. From his office at Yale, librarian Mark Gentry has made online medical resources and textbooks available to Makerere students and faculty in Kampala.

“Through this program we have been able to get a lot of reading materials, which I think makes us better able to look up issues and treat our patients,” said Mulago resident Fred Semitala, M.D., a graduate of Makerere. Semitala would like to see more Ugandans train at Yale. So far, three have traveled to New Haven. “If we train a hematologist or a nephrologist, then that person is going to train five or more,” he says, adding a caveat. “Training without the facilities to use doesn’t help. A cardiologist couldn’t do a better diagnosis if he doesn’t have EKG.”

Ali Moses, one of three Ugandan trainees to come to Connecticut, spent four months at Waterbury Hospital and Yale-New Haven Hospital learning about evidence-based medicine, diagnostic skills and patient management protocols. “The Yale elective provides an opportunity to appreciate the practice of ‘ideal’ clinical medicine, which can be used as a standard or benchmark for and basis for improvement in general clinical care,” he said in an e-mail from Kampala.

Other benefits are intangible yet no less important. A Yale second-year resident, Michael X. Lee, M.D., who was in Uganda last summer, tried to introduce evidence-based medicine while on the wards. Evidence-based medicine, a concept that emerged more than 25 years ago, applies the

latest and best evidence to make medical decisions. “A lot of things are practiced because that is the way it has been practiced for years,” Lee said. “I try to ask the Ugandan residents, ‘What is the evidence for what you just said?’”

“I think where we can really help is in role modeling,” said José Evangelista, M.D., a third-year resident who was at Mulago last summer. “It is my role to help by teaching.”

All the visitors at times felt overwhelmed by the hospital.

“You are frustrated on so many levels,” said Samit Joshi, M.D., a third-year resident. “At a system level you wish the hospital had more free services and more basic tests or better nursing care or better doctor care. At a public health level you wish there were enough prevention campaigns so that people don’t come in with HIV or malaria or schistosomiasis.”

“It is easy to walk into a situation and be overwhelmed. There is also a different way of looking at it,” said Lee. “They save a lot of lives in Mulago. They have treated many people successfully. We have a lot of respect for the people that work here.”

### Life at the Edge

If the Mulago experience caused the residents and students to question what it means to be a doctor, the living arrangements altered the traditional hierarchy of students, residents and attendings. Residents and attendings don’t usually share bedrooms and bathrooms or see each other in shorts and T-shirts every evening. Nor do residents typically see an attending ironing his shirt in the morning. The Mulago setting also made for a round-the-clock learning experience—the talk around the house was usually about medicine.

Home for the Yale team was the Edge Guest House on the 300-acre campus of Makerere University. The walled university, sitting on a hill of the same name, is a haven of calm against the bustle of Kampala, where the air fills with the exhaust of countless *matatus*—minivans that provide public transport—motorcycles and taxis. And the Edge, a complex that includes a six-bedroom house and two smaller outbuildings enclosed inside a wall, provides further insulation from the city.

In the house was a revolving cast of characters that included Sadigh, four residents, two public health students, a physician associate student, a resident from Columbia University, a resident from New York University, and Sadigh’s son, Kaveh, a medical student at Tulane University. A few



One of the goals of the collaboration is to offer Yale attendings, residents and medical students a chance to understand not just Ugandan health care, but also the country's culture and politics. One field trip took medical students to the Patiko-Ajulu Internally Displaced Persons Camp near Gulu in northern Uganda near the Sudanese border. This camp houses about 10,000 people forced to leave their homes by the Lord's Resistance Army, a rebel group that opposes the Ugandan government and is known for kidnapping children to serve as soldiers.

**ABOVE LEFT** Children wandered about the Patiko-Ajulu camp on a weekend in July.

**LEFT** A young woman of 17, a day after giving birth to her son in the camp's clinic.

**ABOVE** The Yale group also visited Kasensero, a fishing village on Lake Victoria, and the epicenter of Uganda's AIDS epidemic. At the local clinic, which has received some support from Yale faculty, villagers offered songs and dances in honor of their foreign visitors.

blocks away most of the team's female contingent—five medical students—shared an on-campus apartment.

Mornings at the Edge began around seven o'clock as residents and students prepared hot water for tea and ate breakfast—avocado sandwiches were one resident's favorite—before heading for Mulago Hospital. The 25-minute walk took the residents and students through the green lawns and crumbling sidewalks of the university to the eastern gate on busy Bombo Road. Traffic lights are almost nonexistent in Kampala. Traffic circles called roundabouts control the flow of vehicles at intersections. Frequent speed bumps on busy roads slow down traffic enough for pedestrians to scurry across.

From Bombo Road the path to Mulago follows a dirt track into a shantytown called Katanga. Although Katanga is safe during the day, the Yale team is advised to avoid the

slum after dark. The path descends into the Katanga valley, past a soccer field, past grazing cows and goats, past a small brick factory, up the dirt track and across another busy thoroughfare to the back entrance of Mulago Hospital.

At the hospital residents and students started the day with morning report. "We find out how the patient is doing. Together we come up with a management plan for the day for the patient. Interspersed with that is the opportunity to do peer teaching," said Lee.

During one day's rounds through the infectious disease ward, Joshi worked with Patrick Komakech, M.D., a Mulago intern, and Rasikh Tuktamysvov, M.D., from Kazan, Russia, who was in Uganda at Sadigh's invitation. Joining the team was Rachel Smith, a fourth-year medical student from the University of California, San Francisco.

The patients included a woman who looked to be a teenager but was 24. She lay on a bed covered only by a sheet, with no attendants to look after her. HIV-positive and anemic, she had been vomiting. The next patient was a 40-year-old woman complaining of vomiting, fever and headache. The differential diagnosis suggested malaria and the doctors administered quinine through an IV. Another patient had good blanket signs—a suitcase for her belongings and an attendant sitting at her bedside with a cup of tea. The patient's diagnosis was cryptococcal meningitis, a common infection in patients with low CD4 counts.

Among the day's patients was a 20-year-old woman with AIDS who had been abandoned by her husband. He had made it clear to the hospital that he didn't want her back. Although she was not sick enough to remain in the hospital, she was too sick to be on her own. A social worker intervened and the husband took her back.

By noon, rounds are usually over and the medical teams break for lunch in the hospital canteen on the second floor. Lunch can be snacks—small pizzas or fried meat pies—or a buffet that offers a heaping plate of rice, sweet potatoes and *matoke* (mashed plantain) covered by a bean, beef or goat stew.

After lunch the residents may perform tasks that usually fall to nurses in the United States, such as drawing blood for tests or removing fluid from patients' abdomens. On-call days are the same, except that between 4 and 5 p.m. they go to the casualty ward and evaluate new patients, determine the primary problem, and triage them to such different services as gastroenterology, infectious diseases, renal, pulmonary, cardiology or neurology.

Two or three evenings a week, Sadigh set up two laptops in the living room of the Edge Guest House for his talks on infectious diseases. He also arranged for classes in Luganda, one of the country's principal languages, talks on Ugandan history by a political scientist and weekend trips to sites of historical and cultural significance.

### A transforming experience

Their experiences in Uganda have already had an effect on the doctors and students. For the students, it has confirmed or altered their career choices—all three medical students have chosen to specialize in internal medicine—and their sense of what is important to learn. And residents find themselves taking a different approach to medicine.

"I think my physical exam skills went through the roof," said Joshi, the third-year resident, a few weeks after his return to Connecticut. "My ordering of tests has probably gone down by 40 percent. If I get this test, X-ray or CT scan—which is hard to come by in Mulago—is it going to give me some new insight that I can't get by putting my stethoscope on the patient's chest?"

And it's not just students and residents starting out in their careers who are affected by the experience. "What does it really mean to be an effective clinician?" asked Mercedes Villanueva, M.D., an infectious disease specialist at Yale-affiliated Waterbury Hospital who spent three weeks at Mulago. In October she addressed a reception to open an exhibit of photographs and essays about Uganda. "From where does a clinician's power ultimately derive? Clearly, we rely on our technical expertise, our knowledge of pathophysiology, our ability to use evidence to make diagnoses and formulate treatment plans. ... But beyond this, I believe our power derives from our ability to listen, examine carefully, synthesize data and draw on our previous experiences."

For Sadigh it's not enough that Yale students, residents and attendings learn how to practice medicine with limited resources. He also wants to purge them of prejudices or paternalism. "We shouldn't be making judgments about a community that is overwhelmed at every level," he says. He expects that the young Yale doctors will learn from the experience, and he acknowledges the difficulties they face—linguistic and cultural barriers as well as patients who have no money for medicines or no one to fetch them a glass of water.

"It is a kind of shock therapy," says Mulago's Opio. "Most people do not know what happens in the developing world. ... Many of them are going to become great people in their lifetimes, but I think their experience here will make them better people."

That is also the hope that drives Sadigh.

"At the end of the trip they will be different people," he says. "I can't measure that, but I think they will be different people. ... If they become better people, in the future I think Uganda is going to gain a lot from this. That is a long-term investment."

John Curtis is the managing editor of *Yale Medicine*.

## Uganda clerkships inaugurate a new foreign electives program

After six weeks in Uganda last summer, fourth-year medical students Allison Arwady, Lily Horng and Rachel Laff said the clinical rotation at Mulago Hospital was the best they'd had in medical school. The three were the first students to travel abroad with support from three new fellowships endowed by alumni donations. The fellowships marked the beginning of an ambitious program to support international clerkships for students.

"This is different from anything that has ever happened before," said Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93, associate dean for student affairs. Students have long traveled abroad for clerkships,

but at their own expense. For the first time, the medical school is offering financial support. Angoff believes the experience in a foreign hospital will have a lasting and positive influence on the students' development as doctors.

Arwady, Horng and Laff joined an existing medical exchange led by Majid Sadigh, M.D., associate professor of medicine. This was the first time that the exchange, which has brought Yale residents to Uganda since the summer of 2006, hosted medical students.

"It was hard," said Arwady, who had previously been in South Africa and Botswana, working on projects as a medical student. "It was also one of the most intense and thought-provoking experiences I have had in years.

You are out of your comfort zone in every way."

"I learned a lot, thanks to the residents and most of all to Dr. Sadigh," said Laff, who had previously spent three months in Gabon. She said her time in Uganda reinforced her decision to pursue internal medicine. "I want that broad training," she said.

"It was the best rotation I've had, hands down," said Horng, who had previously traveled to China and Chile.

On Mulago's wards they saw the limitations of medicine in a developing country and marveled at the skills and knowledge of their Ugandan colleagues. They came away with a heightened appreciation of the importance of the physical exam, which they saw their Ugandan and Yale colleagues relying on for diagnoses. "It's something that we don't do that well here," said Arwady.

Also in Uganda was Matthew S. Cook, PA '07, then in his final year of the Physician Associate Program, which provided partial support for his rotation. Like the medical students, he said his experience in Uganda left a lasting impression. "I definitely have a commitment to do medicine overseas," he said. Cook began a two-week rotation on the Community Health Care Van on his return to New Haven. Coming on the heels of his Uganda clerkship, the van rotation made him more aware of health disparities in this country. "The health care system is broken and flawed. The problems are so widespread there is no easy fix," said Cook, who is now on the hospitalist service at Yale-New Haven Hospital.

Robert M. Rohrbaugh, M.D., associate professor of psychiatry, and administrator for the clinical elective program that has brought foreign students to Yale for electives, said the success of the Ugandan program bodes well for future foreign electives.

"Despite the difficulties that everyone that goes there encounters, it was confirmatory for them that this is what they want to do," he said.

Foreign electives will be open to students who have completed their third year. In addition to the six-week clerkships, students can apply for the year-long Yale-China Medical English Fellows Program. Nancy Chapman, executive director of the Yale-China Association, said the fellows going to China would teach medical English and study Mandarin, the official modern spoken language of China. They would also have clinical and research opportunities. The association will pay travel expenses and provide a stipend and housing at the Xiangya School of Medicine in Changsha, Hunan.

Wherever they go, students would be expected to learn about the host country and learn something of the language. "They have to be prepared," Angoff said. "They will also have an opportunity to debrief afterwards, as these experiences can be emotionally charged."

Rohrbaugh said students will benefit in several ways. "They'll be able to practice what they've learned at Yale in different settings. They'll be seeing patients with different presentations of illness. They'll develop an awareness of the social and political factors in health and disease," he said. "There is a basic cultural competency that you learn."

—John Curtis



A podcast of Robert Rohrbaugh speaking on this subject can be found on the Yale page on iTunes U. Visit [itunes.yale.edu](https://itunes.yale.edu) or launch iTunes, then select Yale from the offerings under iTunes U. The podcast is included under "Yale Health and Medicine."







By Colleen Shaddox and Michael Fitzsosa  
Photography by Frank Poole

# A tale of two doctors

First as student and teacher, then as colleagues, and now as co-authors, a cardiothoracic surgeon and a cardiologist have worked side by side at Yale for 30 years. **John Elefteriades**, head of cardiothoracic surgery, and **Lawrence Cohen**, the former special assistant to the dean, recently published *Your Heart: An Owner's Guide*, which explains cardiac problems and how to treat them.

## John Elefteriades

The walls of his office are lined with a variety of “Best Doctor” magazine covers and plaques from professional societies. But John A. Elefteriades, M.D. '76, HS '81, FW '83, directs visitors' attention only to the framed pages closest to his desk. They are thank-you letters and drawings from patients, famous and less well-known, whom he has saved in the operating room. Congratulate Elefteriades on one of his latest accolades, being named the William W.L. Glenn Professor of Cardiothoracic Surgery in 2006, and he'll smile slightly and call the appointment “some kind of clerical error.”

Cardiologist Lawrence S. Cohen, M.D., HS '65, the Ebenezer K. Hunt Professor of Medicine and a longtime mentor and collaborator, sets the record straight. Glenn, who died in 2003, was a pioneering surgeon, head of the cardiothoracic section for decades, and one of Elefteriades' teachers. “He was very proud of John and hoped that after

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## Lawrence Cohen

When Jeffrey R. Bender, M.D., HS '83, met Lawrence S. Cohen, M.D., HS '65, in the early 1980s, Bender was a resident in internal medicine and Cohen introduced Yale medical students and residents to cardiology. Deliberate, concise and impeccably dressed in a blazer, collared shirt and cuff links, never a crease out of place, Cohen was one of those professors whom students honor with a nickname.

“He was known as ‘Larry the Heart,’ ” recalls Bender, now the Robert I. Levy Professor of Preventive Cardiology and professor of medicine and immunobiology, “and he was the consummate teacher.”

At 74, Cohen, the Ebenezer K. Hunt Professor of Medicine, is still the expert from whom every Yale medical student learns how to listen for and interpret heart sounds. He estimates that he's taught some 3,000 students over the past 35 years. But that facet of his academic life represents just a fraction of his contributions to Yale, to medicine

*continued on page 34*

**John Elefteriades, left, and Lawrence Cohen, have a lot in common. Both are renowned in their fields, cardiothoracic surgery and cardiology. Both have conducted groundbreaking research. And both are known as consummate teachers.**

# Elefteriades

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the chair was established that John Elefteriades would be its first incumbent,” Cohen said.

Elefteriades has done groundbreaking research on aortic aneurysms—weakened areas in the wall of the heart’s main artery—and is sought out by millionaires and royalty for his surgical skills. But Cohen says patients are just as often moved by “his gentleness.” Patients like Carmela Kolman.

Kolman was 32, an artist who knew that she had an aortic aneurysm and that it meant surgery at some point in her future. The future came crashing down on her, however, one Saturday morning in 1993 when the three layers of tissue comprising her aorta were forced apart by the pressure of the blood inside the vessel and the aneurysm dissected. She crawled to the telephone and whispered to the 911 operator, “Pain. In my chest.”

Elefteriades repaired her aorta and became a “calm, reassuring presence” in the weeks that followed, both for Kolman and her husband, John A. Rizzo, PH.D., a health economist then on the faculty of the Department of Epidemiology and Public Health. Together Rizzo and Elefteriades embarked on a course of research that continues to improve care for patients like Kolman.

Despite the danger of aortic aneurysms, physicians balk at performing open-heart surgery unless the aneurysm is at immediate risk of dissecting or bursting. But if the aneurysm does dissect or burst, mortality skyrockets. The key is determining the right moment to operate. There were few tools to predict when an aneurysm would reach a crisis stage until Elefteriades and Rizzo developed the largest aortic aneurysm database in the world, with 3,000 cases. In the past 15 years, their research has identified the risk factors that put patients with aneurysms in imminent danger.

Rizzo, now at the State University of New York at Stony Brook, jokes that Elefteriades is “the only person I’ve ever worked with for an extended period of time who has never lost patience with me.” But he goes on to say that Elefteriades never loses patience, period. When the data are perplexing or a journal imposes an impossible deadline, Elefteriades maintains perfect composure, Rizzo says, and the calm is contagious. “That’s what I call a leader,” he adds.

Elefteriades also collaborates with the Celera Group, the private firm that engaged in a scientific race with the government’s Human Genome Project. Together they’ve identified genetic alterations associated with aneurysms



and, by examining a patient’s RNA, can predict whether a patient will develop an aneurysm. (Their findings were published in the October 17 issue of *PLoS ONE*.) The test is 85 percent specific and close to 100 percent accurate, meaning that positive results accurately predict the development of aneurysms while about 15 percent of the patients on track for an aneurysm will test negative. DNA analysis that could complement the RNA findings is under way, and Elefteriades hopes the test will be widely used in high-risk patients.

His research has also taken him into the twilight zone where patients hover on life’s threshold. To operate on the aortic arch—the area usually clamped off when a patient is put on a heart-lung machine—blood circulation is suspended by inducing hypothermia. When a patient’s body cools to 18 degrees Celsius (about 64.4 degrees Fahrenheit) and the metabolic rate slows to 12.5 percent of normal, Elefteriades has 30 to 60 minutes to repair an aneurysm on the aortic arch. His patients have neither blood pressure nor pulse; they are “for all intents and purposes, dead,” says Elefteriades. They awake with no apparent loss of memory or cognitive function.

“I’ve done [the operation] probably as much as anyone has done it,” says Elefteriades. “And I don’t understand it. I’m awed by it.”

He wants to know why these patients thrive after a brush with death. He has an undergraduate interviewing 75 patients and their spouses in search of “subtle aberrations” in the patient’s behavior after the surgery. The patients selected for the study have varied but mentally demanding occupations: there are lawyers, doctors, artists and financial analysts in the sample. The study found no decline whatsoever in their functional state after deep hypothermic arrest, Elefteriades said.

Elefteriades continues to publish on the health risks of an exercise he enjoys himself, weight lifting. He has seen patterns in sudden deaths among high school and college athletes who lift weights, an exercise Elefteriades first took up as a high school wrestler. He reviewed cases of 31 young men who had died when their undetected aortic aneurysms dissected. He is recommending echocardiograms for all weight lifters to screen for aneurysms. Elefteriades acknowledges that the recommendation drives up health care spending but says, “I don’t know any other way to keep these kids safe.”

## “The operating room is like a drug. If I’m away for a week I feel like I haven’t contributed to humanity.”

His research tends to spring from clinical questions, so in a sense the surgeon’s own heart never quite leaves the operating room. “The operating room is like a drug,” he says. “If I’m away for a week, I feel I haven’t contributed to humanity.”

Ironically, the career that inspires such passion in him was the result of happenstance.

A top student and serious wrestler on the high school team in Lansdowne, Penn., Elefteriades had been accepted to the Massachusetts Institute of Technology. He was planning to be an engineer, much to the pride and delight of his immigrant parents, who had not gone to college themselves. One day a Yale recruiter walked into his classroom and declared, “Young man, you’re going to Yale.”

Elefteriades says he does not know what piqued the recruiter’s interest—perhaps a chat beforehand with the friendly principal. Whatever the reason, he is grateful that fate steered him to New Haven.

At Yale, his horizons widened. “I think it’s the best place to go to college that there is,” Elefteriades remembers. Yale allowed him to follow his varied interests: French literature, physics, psychology. It wasn’t fashionable to have a career path in mind in the early seventies, he recalls. So he began taking exams for various graduate and professional programs. He ended up in medical school because the MCATs were the first set of results he got back.

He explains his choice of surgery as motivated by “a love of the beauty of the body, and the body really is beautiful—internally, externally.” He remembers the world of cardiothoracic surgery in the 1970s being relatively new and full of challenges. While much of his work involves expanding the discipline’s knowledge base, he is equally satisfied performing bypass surgery, though he’s done the procedure thousands of times. “Each case is a little different. Every blood vessel is a little different,” he says.

In addition to his scholarly work, Elefteriades writes for the lay public, a pursuit he finds “relaxing.” He co-authored *Your Heart: An Owner’s Guide* with Cohen, a work that explains cardiac problems and their treatment. Both writers said the book is in part a response to the time pressure exerted by health management organizations that frequently robs patients and families of the chance to ask detailed questions of their physicians. A second book, *The Woman’s Heart: An Owner’s Guide*, is in press. Elefteriades,

who co-authored the book with Teresa L. Caulin-Glaser, M.D., HS ’91, FW ’95, a clinical associate professor of internal medicine at Ohio State University, hastens to explain that he’s demystifying the female heart from a medical perspective, not a poetic one. “If I could understand the woman’s heart, that would be great,” he says. “I think women are much more complex and interesting than men—emotionally and in nearly every other way.” He also has a book on cardiac fitness in the pipeline and another of patient stories, titled *Extraordinary Hearts*.

He attributes his productivity to a “phenomenal” support staff and a changing corps of students and residents who do much of the heavy lifting in his research. “My role as a mentor is to identify a topic that is an important open question,” says Elefteriades, and then to offer guidance on how to write a scientific paper. He finds that students “usually exceed any expectations I could have for them.”

Elefteriades received the Socrates Award for Excellence in teaching and mentoring of residents from the Society of Thoracic Surgeons in 2006. He calls his impact as a teacher his proudest achievement and points to the former Yale residents who are now directing cardiac centers.

It is especially gratifying to bring a medical student into the operating room for the first time and hear, “This is the greatest day of my life!” That was how Elefteriades felt his first day in surgery. The feeling has lingered.

Colleen Shaddox is a freelance writer in Hamden, Conn.

# Cohen

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and to the advancement of cardiac care during a career that began with his graduation from New York University Medical School in 1958.

It's advancement of patient care that fills Cohen with satisfaction and even a sense of wonder when he thinks back to the early days of his academic career. "The number one difference between then and now is that someone practicing now has the tools to prevent heart disease," he says. That we have this armamentarium at all is in part thanks to Cohen. The Brooklyn-born cardiologist was a key player in the major studies that established the efficacy of clot-busting medications to stop heart attacks and slow the hardening and clogging of the arteries that usually precipitate coronary disease. Cohen was the principal investigator at Yale of a series of multicenter trials of thrombolytic drugs, including streptokinase and tissue plasminogen activator, or t-PA. These drugs dissolve blood clots by harnessing an enzyme called plasmin to break down fibrin, the protein that helps platelets bind to form a clot. These early Thrombolysis in Myocardial Infarction (TIMI) trials in the late 1980s proved that thrombolytics would help patients who were experiencing an acute myocardial infarction, an interruption of blood flow to the heart muscle. Since the mid-1970s, Cohen has overseen some two dozen trials of heart disease treatments, some of them ongoing.

Because of his wide experience and calm, effective approach to decision making, Cohen's advice has been sought for years. Students, residents, fellows, colleagues in cardiology and deans trust his judgment, and not only about medicine. In 1991, then-Dean Leon Rosenberg, M.D., HS '63, asked him to serve as his deputy dean. Cohen continued in that role under Robert Donaldson, M.D., and Gerard Burrow, M.D. '58, HS '66. For the past 10 years he has been the special advisor to three deans, David A. Kessler, M.D., Interim Dean Dennis D. Spencer, M.D., HS '77, and current Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. Cohen's focus has ranged from overseeing faculty appointments and promotions to raising money for endowed professorships to investigating scientific misconduct and fraud. Of the latter, Cohen says, "It doesn't happen very often, but when it does the university takes it very seriously."

With his colleague Merle Waxman, M.A., the medical school's ombudsperson, Cohen took a preventive approach to research misconduct. They developed a seminar series



titled "The Responsible Conduct of Research," which has been presented to more than 1,000 postdoctoral fellows, graduate students and faculty since 1996. Most allegations, Cohen believes, can be avoided by taking a few precautions, and he advises faculty to be open and communicative about their research from the earliest stages of a project. Meticulous and transparent data recording, frequent meetings with collaborators and familiarity with all aspects of a project, not just one's own part in it, he says, are the keys to avoiding problems down the road.

After 16 years, Cohen stepped down from his role as the dean's advisor last July, but he is continuing as a full-time faculty member and practicing cardiologist. "I'm not retiring," he told colleagues and acquaintances in the weeks leading up to a May 1 reception in his honor in the Medical Historical Library. As word of the reception spread, Cohen found himself explaining again and again that he was not leaving Yale.

"I hear you're retiring," Don McNulty, a maintenance worker that Cohen has known for 30 years, said a few days before the ceremony, which was attended by more than 100 colleagues, family members and friends, including Yale President Richard C. Levin and Yale-New Haven Hospital CEO Marna P. Borgstrom, M.P.H. '79.

"I'm not retiring," Cohen said for the umpteenth time, his face betraying not a hint of impatience. "I'm just leaving the dean's office. I will still be here."

That's good news for the medical school, says longtime collaborator John A. Elefteriades, M.D. '76, HS '81, FW '83, the section chief and William W.L. Glenn Professor of Cardiothoracic Surgery. Elefteriades, who learned from Cohen to listen to the heart as a medical student, calls his mentor "the cardiologists' cardiologist."

"When any of us is ill, we go to him," he says of Cohen. "Both my parents see him. Whenever there's a tremendously difficult or complex case that requires exceptional judgment, cardiologists from all over the region will send their patients to him."

In 2007 Elefteriades and Cohen published their second book together, *Your Heart: An Owner's Guide* (Prometheus Books), with a foreword by artificial heart inventor Robert Jarvik, M.D. It is Cohen's fourth book—he has also published 34 book chapters and 136 papers.

## “He doesn’t go through the motions, but focuses entirely on each patient and he finds things that other doctors don’t find.”

Cohen is married to Jane A. Cohen, M.S.W., a psychiatric social worker in private practice, and has two daughters and four grandchildren. He grew up in the Flatbush section of Brooklyn, N.Y., the youngest of three children. His grandparents were emigrants from Poland and Russia; his father owned a chain of men’s clothing stores. Cohen attended Midwood High School in Brooklyn and then Harvard College, graduating in 1954 with a degree in social psychology. After medical school at NYU, he came to Yale in 1958 as an intern in medicine and stayed for a second year as a resident before joining the U.S. Public Health Service as a research fellow in infectious diseases. After two years as a research fellow in cardiology at the Peter Bent Brigham Hospital in Boston, he returned to Yale as a senior resident in 1964-65.

His mentors were Paul B. Beeson, M.D.; Eugene Braunwald, M.D.; and Donald W. Seldin, M.D. ’43, HS ’46. Cohen remembers Beeson, a legendary chair of medicine at Yale who conducted research on fever and discovered the class of signaling molecules called cytokines, as “a quiet, charismatic man who led by making you want to do your very best.

“You never wanted to disappoint Paul Beeson. He really cared about the care of the patient and would sit down on the bed and talk directly to the patient, which was very unusual in that day,” Cohen says. Braunwald, author of the leading cardiology text, *Heart Disease*, and chair of the TIMI Study Group at Brigham and Women’s Hospital, recruited Cohen to the cardiology branch of the National Heart Institute, where Cohen served as chief of the clinical service. He would go on to work with Braunwald on the first three TIMI studies, which proved that heart attacks are caused by the rupture of plaque from the wall of an artery, followed by clotting.

“It was the clot that stopped the blood flow and caused the death of heart muscle,” says Cohen. “TIMI proved that if you could dissolve the clot in a timely fashion and thereby re-establish blood flow to the heart muscle, you could limit or prevent the effects of a heart attack completely.”

Seldin, who left a comfortable teaching post at Yale to build a research powerhouse at the University of Texas Southwestern Medical School, recruited Cohen to Dallas. After two years, Cohen was lured back to Yale in 1970 as chief of cardiology.

Trained by giants in medicine, Cohen has himself mentored dozens of influential cardiologists and leaders in academic medicine, including Kim A. Eagle, M.D., HS ’83, director

of the Cardiovascular Center at the University of Michigan; and John M. Lasala, M.D., PH.D., FW ’90, director of interventional cardiology at Washington University in St. Louis.

Lasala, who came to Yale as a cardiology fellow in 1986, remembers being impressed by Cohen’s ability to find the most salient and critical details in a mass of complex information. “He obviously knew quite a bit, but the most amazing thing was his ability to synthesize great amounts of information into simple and factually correct assessments,” says Lasala. He recalls examining a patient who had been seen in the practice 20 years previously. “Whose notes do you think were in the chart?” Whereas some of the notes would run to two or three pages, he says, “Larry’s notes were three lines—but much more informative. They were so pithy and to the heart of the matter—no pun intended—that you couldn’t fail to be impressed. He could say an awful lot with very little.”

Eagle recognized this ability as well, along with Cohen’s penchant for relating to patients. “He’s brilliant,” Eagle says. “He doesn’t go through the motions but focuses entirely on each patient, and he finds things that other doctors don’t find. He’s meticulous, not only in his speech, dress and manner, but in his physical examination. He’s like a laser-guided missile when it comes to finding a problem.”

Cohen is looking forward to his continued work with patients, students and trainees and his work on the medical school’s admissions committee, on which he has served for the past six years. He’ll continue teaching for the satisfaction of inspiring young people and watching them grow, he says, and he’ll remain active academically because of the stimulation it provides. “The collegiality and contact with people who are pushing the frontiers of science—that is a very good feeling,” he says.

But his voice takes on a tone of reverence when he speaks of his work in the clinical realm.

“Being able to make a difference in patients’ lives,” Cohen says, “is a privilege.”

Michael Fitzsosa is director of communications in the medical school’s Office of Institutional Planning and Communications.



Benjamin Bunney

## Retiring chair of psychiatry honored

Measuring the legacy of a scientist with a 38-year career can take many forms—tallies of awards, peer-reviewed publications or citations of papers. But to grasp his impact as a leader, colleague and mentor, one need look no further than his students.

On July 12, students and colleagues of **BENJAMIN S. BUNNEY, M.D.**, the Charles B.G. Murphy Professor of Psychiatry and professor of pharmacology and neurobiology, showed that Bunney's legacy will live on at universities around the world long after his retirement from Yale this year.

Bunney, known to colleagues as Steve, has spent 40 years at Yale, the past 20 as chair of psychiatry. One of the world's leading authorities on the neurotransmitter dopamine, he has made fundamental contributions to the study of the regulation of dopamine neuronal systems and the effects of antipsychotic drugs on the brain. The July symposium in Bunney's honor brought together students and colleagues who carry on the themes of his research.

"You can't mention the dopamine system without mentioning his seminal work," said Tony Grace, **PH.D.**, the first graduate student to work in Bunney's lab and now a professor of neuroscience, psychiatry and psychology at the University of Pittsburgh.

Bunney's pioneering experiments, first carried out in the 1970s under the mentorship of George K. Aghajanian, **M.D.** '58, **FW** '63, the Foundations Fund Professor of Psychiatry, recorded the extracellular activity of dopamine neurons in the brain for the first time. Bunney's laboratory then went on to identify them

and characterize both their extra- and intracellular functioning. Disruptions of the dopamine system have been linked to schizophrenia, Parkinson's disease, attention-deficit hyperactivity disorder and drug abuse. Much of Bunney's career was spent probing the dopamine-schizophrenia link; and his work, combined with the contributions of others, helped lead to a new generation of antipsychotic drugs.

Paul Greengard, **PH.D.**, the Vincent Astor Professor at Rockefeller University, winner of the 2000 Nobel Prize in physiology or medicine for his dopamine research, a former professor of pharmacology and psychiatry at Yale and early collaborator with Bunney, led off the day with a discussion of his work. Greengard has shown that dopamine and other neurotransmitters can activate a key protein known as **DARPP-32**, which in turn influences the functioning of nerve cells.

At the end of the day, Bunney spoke modestly of his own career, calling every symposium speaker "a pioneer in their own area."

"I'm going to miss being a scientist and I'm going to miss being at Yale enormously," said Bunney. The audience responded with thunderous applause and a standing ovation. "You can never repay your own mentors enough," Bunney said, "but you can pass along what you've learned to the next generation."



Robert Alpern



Harlan Krumholz



Mary Tinetti



Erol Fikrig

## Three faculty named to IOM in 2007

Three Yale faculty members were named to the Institute of Medicine (**IOM**) in October, bringing the total from the university to 42.

Among the 65 new members inducted this year were Dean **ROBERT J. ALPERN, M.D.**, Ensign Professor of Medicine; **HARLAN M. KRUMHOLZ, M.D.**, the Harold H. Hines Jr. Professor of Medicine and professor of epidemiology and public health and of investigative medicine; and **MARY E. TINETTI, M.D.**, the Gladys Phillips Crowfoot Professor of Medicine and professor of epidemiology and public health and of investigative medicine.

Alpern is a nephrologist whose research has focused on the regulation of kidney transport proteins. Before coming to Yale, Alpern was dean of the University of Texas Southwestern School of Medicine.

Krumholz, the director of the Robert Wood Johnson Clinical Scholars Program, is noted for research aimed at determining optimal clinical strategies and identifying opportunities for improvement in the prevention, treatment and outcome of cardiovascular disease. His research group has pioneered innovative approaches to identifying key success strategies for top-performing health care organizations and translating the knowledge into practice.

Tinetti is the director of the Yale Program on Aging. Her recent work focuses on the effect of multiple diseases on health outcomes and on appropriate decision making in the face of multiple competing diseases. She has been the director of the Claude D. Pepper Older Americans Independence Center at Yale since 1992.

## Lyme disease expert to lead ID section

**EROL FIKRIG, M.D.**, **FW** '91, an expert in vector-borne diseases and a pioneer in the development of a vaccine for Lyme disease, has been named chief of the Section of Infectious Diseases in the Department of Internal Medicine. Last fall he was also named a Howard Hughes Medical Institute (**HHMI**) investigator.

Fikrig, recently named Waldemar Von Zedtwitz Professor of Medicine, succeeds Acting Chief Vincent J. Quagliarello, **M.D.**, **HS** '81, professor of medicine and clinical director of infectious diseases. Fikrig graduated from Cornell University's school of medicine and completed his residency in internal medicine at Vanderbilt University Hospital. He came to Yale as a postdoctoral fellow in infectious diseases and immunobiology in 1988. He was appointed assistant professor of medicine in 1992 and professor of medicine a decade later.

**JACK A. ELIAS, M.D.**, chair and Waldemar Von Zedtwitz Professor of Medicine, called Fikrig a "world-class scientist" and one of the "world's experts" in Lyme disease and West Nile virus. Under Fikrig's leadership, the section will place greater emphasis on developing a program in emerging diseases, vaccines and biology. This effort will include hiring at least four investigators with strengths in basic science, translational research and clinical research. The goal is to cultivate an interdisciplinary community of scientists who will use information gathered at the bedside to develop models in the laboratory for testing new therapies, including vaccines to prevent insect-borne infectious diseases.



Richard Belitsky



James Duncan



Linda Mayes



Derek Toomre



Kyle Vanderlick

Four medical school faculty members have been named to endowed chairs. **Richard Belitsky**, M.D., deputy dean for education, has been named the Harold W. Jockers Associate Professor of Medical Education. Belitsky served as the director of graduate education in the Department of Psychiatry from 1996 to 1997 and as the department's director of education from 1997 to 2006. He has earned numerous professional honors at Yale, including the Charles W. Bohmfalk Teaching Prize and the Francis Gilman Blake Award. **James S. Duncan**, PH.D., was named the Ebenezer K. Hunt Professor of Biomedical Engineering in September. Duncan is the associate chair and director of undergraduate studies in the Department of Biomedical Engineering as well as the vice chair for bioimaging sciences research in diagnostic radiology. **Erol Fikrig**, M.D., an expert in such vector-borne diseases as Lyme disease, human granulocytic ehrlichiosis and West Nile virus, has been named Waldemar Von Zedtwitz Professor of Medicine (See opposite page). **Sally Shaywitz**, M.D., has been named the Audrey Ratner Professor in Learning Development. Shaywitz is the co-director of the newly formed Yale Center for Dyslexia and Creativity and the Yale Center for Learning, Reading and Attention. Her research pioneered the use of functional magnetic resonance imaging in investigating reading disorders.

**Henry J. Binder**, M.D., professor of medicine and of cellular and molecular physiology, received the 2007 Distinguished Mentor Award from the American Gastroenterological Association in May.

This award recognizes individuals who have made lifelong efforts to mentor trainees in gastroenterology. Binder established the Gastrointestinal Research Training Program at Yale and is the program's director.

**Robert Dubrow**, M.D., associate professor in the Division of Chronic Disease Epidemiology and director of the Office of International Training at Yale's Center for Interdisciplinary Research on AIDS, has been named associate dean for academic affairs at the Department of Epidemiology and Public Health. In this newly created position, Dubrow will oversee and coordinate the educational curriculum, chair the education committee and help develop an office of public health practice to offer M.P.H. students practice experience and internships around the world.

**Linda C. Mayes**, M.D., the Arnold Gesell Professor of Child Psychiatry in the Child Study Center and professor of pediatrics and psychology, has been named Special Advisor to the Dean as of July 1. Mayes will be responsible for the oversight of scientific integrity in research conducted at the School of Medicine and for the investigation of any allegations of scientific misconduct. In addition, the special advisor often acts as a mediator when there are substantive faculty issues regarding authorship. Mayes will also function as the dean's representative in hearing grievances by faculty and students regarding appointments, promotions and terminations.

Mayes joined the faculty of the Yale Child Study Center in

1985. Her work focuses on the stress-response and emotional regulatory mechanisms in children and adolescents at both biological and psychosocial risk. Mayes chairs the directorial team of the Anna Freud Centre in London and of the Anna Freud Centre program within the Child Study Center at Yale.

**Susan T. Mayne**, PH.D., professor in the Division of Chronic Disease Epidemiology in the School of Public Health, has been appointed to a three-year term on the Institute of Medicine's Food and Nutrition Board. The board makes recommendations on ways to improve food quality and safety to prevent diet-related diseases and promote public health.

**Pasquale Patrizio**, M.D., professor of obstetrics, gynecology and reproductive sciences, has been elected to serve as president of the Fertility Preservation Special Interest Group of the American Society for Reproductive Medicine. His term began in October.

**David M. Rothstein**, M.D., associate professor of medicine, has been elected a councilor-at-large of the American Society of Transplantation, an international organization of more than 2,700 transplant physicians, surgeons and allied health professionals dedicated to advancing the field of transplantation through research, education, advocacy and organ donation.

**Derek K. Toomre**, PH.D., assistant professor of cell biology, has received a \$2.5 million five-year New Innovator Award from the National Institutes of Health. Toomre will use the funding to develop a new generation of

total internal reflection fluorescence microscopes to analyze trafficking and signaling at the cell cortex, a structure inside the cell membrane involved in the cell's mechanical support and movement. Toomre's group will apply this technology to understand the trafficking pathways that regulate insulin-stimulated delivery of glucose transporters to the cell surface—a process disrupted in type 2 diabetes.

**Kyle Vanderlick**, PH.D., has been appointed dean of the Yale Faculty of Engineering and named the Thomas E. Golden Professor of Engineering. Vanderlick, formerly professor and chair of chemical engineering at Princeton University, started at Yale on January 1.

Her research has led to fundamental insights in areas ranging from metallic adhesion in micro/nanoscale devices to the action of antimicrobial peptides on cell membranes. In 2002 she was awarded both the Princeton Engineering Council Teaching Award and the Princeton President's Award for Distinguished Teaching.

Vanderlick succeeds **Paul A. Fleury**, PH.D., the Frederick W. Beinecke Professor of Engineering and Applied Physics and professor of physics. Fleury will remain the director of the Yale Institute for Nanoscience and Quantum Engineering.

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## Yale system remains a strong draw

Incoming students cited the quality of faculty, research opportunities and the thesis requirement.

Kwame and Kofi Atsina went to different colleges and have different interests, but when it came time to apply to medical schools, both put Yale on their lists. In September the brothers from Ghana were among the 100 first-year students in the Class of 2011 at the White Coat Ceremony, the annual event that welcomes students to the field of medicine.

“I never knew that we’d end up at the same school,” said Kwame, who attended Lehigh University. “I never guessed we could be so fortunate.”

“I’ll want to know where he is and what he’s doing, but I have to give him space. He’s an adult now,” said his big

brother Kofi, who is 15 months older and graduated from Yale College.

Director of Admissions Richard Silverman said the Atsinas aren’t the first sibling pair to be admitted to the medical school in the same class, but he agrees the odds are long—especially this year. Silverman said the school received 4,056 applications for 100 slots, the highest number in the school’s history and a 9.7 percent jump over last year.

As always, the Yale system remains a big attraction for incoming students. According to a survey Silverman conducted, students said it was their main reason for choosing Yale. They also cited the school’s reputation, research opportunities, the quality of faculty and students and the requirement to write a research thesis.

“High school was very competitive,” said George Hauser. “I wanted to learn for the sake of learning.”

“I fell in love with the vibe,” said Melanie Johncilla. “The lack of competition. The spirit of teamwork.”

In his opening remarks at the ceremony, Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, said that the Yale system didn’t dispense with grades and rankings to make it easier for students. “We expect greater things from you than grades,” he said. “We expect you to become leaders in the medical world.”

—Jennifer Kaylin



**ABOVE** Forrester Lee helped Kofi-Buaku Atsina don his white coat at the annual ceremony in Harkness Auditorium.

**RIGHT** Among the top reasons for choosing Yale, a survey of the 100 incoming students found, were the Yale system, the school’s reputation and the quality of faculty and students.



**ABOVE** After the ceremony students posed for a group photograph outside the Sterling Hall of Medicine.



TERRY DAGRADI (3)



## Response to patients matters most, neurosurgeon tells Physician Associate grads

Twenty years ago Alfredo Quiñones-Hinojosa, M.D., was a 19-year-old illegal immigrant who spoke no English and picked tomatoes in California's San Joaquin Valley. On October 16 he gave the Commencement address to the 33 members of the Physician Associate Class of 2007, speaking as a renowned neurosurgeon and faculty member at Johns Hopkins University School of Medicine.

His path into medicine started with an industrial accident—he fell into a tank car that was used to carry liquefied petroleum gas. When he regained consciousness in the hospital and saw the man in the white coat, he said, “I felt a sense of security that a doctor was taking care of me.” His future, he decided, lay in health care. After attending San Joaquin Delta Community College in Stockton, Calif., and the University of California at Berkeley, he eventually graduated from Harvard Medical School. Quiñones-Hinojosa now directs the Brain Tumor Surgery Program at the Johns Hopkins Bayview Campus.

In his address, Quiñones-Hinojosa wove together the story of his own transformation from immigrant to surgeon with the awe he still feels at the power of his relationships with his patients. Referring to one patient, he said, “Imagine the trust he was putting in me at that moment.” In a talk that referred to Albert Einstein, Martin Luther King Jr., Mohandas Gandhi and Cesar Chavez, among others, he said, “It is not intellect that makes a great scientist, but character; and more than

knowledge, it is the response to patients that matters most. ... Remember, graduates—this is a very important lesson; there is a fine line between confidence and arrogance.”

Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, told the new physician associates, “It is clear that the need for health care is so huge that you will become an increasingly important part of it.” He urged them to help their patients attain and maintain their health; to remain committed to lifelong learning and compassion; and to strive to become leaders in their field.

Student awards went to Deborah B. Cole, PA '07, who received the Academic Achievement Award; Elisabeth M. Samels, PA '07, who received the Clinical Excellence Award; and Matthew S. Cook, PA '07, who received the Dean's Humanitarian Award.

The Didactic Instruction Award for dedication and excellence went to Jeffrey

**BELOW** Alfredo Quiñones-Hinojosa told the physician associate graduates of his rise from undocumented farmworker in California to neurosurgeon at Johns Hopkins University.



E. Topal, M.D., clinical instructor in medicine and infectious diseases, known to students as the “antibiotic guru” of the pharmacology and microbiology courses. The Clinical Site Award, for a clinical rotation site that provides exemplary clinical teaching, was given to the Bridgeport Hospital Department of Emergency Services. The Jack W. Cole Society Award, for significant contributors who support the physician associate profession, was given to William L. Cushing, PA '02, clinical instructor in medicine.

—Jill Max



**ABOVE** Jesse Harkness and Deborah Cole, left, and Timothy Graves and Adam Kelly, right, before the ceremony in Woolsey Hall.

**RIGHT** Clockwise from top left, Christopher Maio, Jacob Hauptman, Jesse Harkness, Maria Clough and Marlene Brodka joined their classmates for a group photo before Commencement.





U.S. SENATE PHOTO STUDIO

As a resident in orthopaedic surgery at Yale, John Barrasso learned the importance of planning ahead, a lesson that has served him well in medicine and politics. In 2002 the Republican won a seat on Wyoming's state senate and last fall he was appointed to fill a vacancy in the United States Senate.

## Surgeon, rodeo doctor and, now, senator

Former Yale resident John Barrasso is named to fill a senate vacancy.

**John A. Barrasso, M.D., HS '83**, the new Republican U.S. senator from Wyoming, recalls that when he was a resident at Yale from 1978 to 1983, his professors stressed the importance of having a plan before going into surgery. "They would tell us that if you don't have a plan to begin with on how to solve the problem, you'll have a much tougher time halfway through the operation," he said.

This advice has served Barrasso well both as an orthopaedic surgeon and as a politician and civic activist. Early in his career, Barrasso's plan was to provide health care for as many people as possible inside and outside the operating room. That plan culminated on June 25, when he was appointed by Gov. David Freudenthal to fill the U.S. Senate seat vacated by the late Craig Thomas. "Affordable and available health care is a big issue in Wyoming," he said. "It's a rural state, and people are spread out. I want to help find ways to get health care to them."

As a medical student at Georgetown University, Barrasso was already thinking about ways to broaden his impact on the public's health care needs. He joined the American Medical Student Association, where he worked on issues related to preventive medicine and health care access.

He produced television and radio reports and newspaper articles on health and fitness for more than 20 years, and served as the medical

director of Wyoming Health Fairs, a series of programs on preventive medicine held across the state. He presently writes a monthly series of articles on preventive health care for elders called "Caring for Wyoming's Seniors." He has also served as a rodeo physician for the Professional Rodeo Cowboys Association and as a sports team physician for Casper College. In 2002 he ran for a seat in the Wyoming State Senate. "I knew I could help patients one-on-one in the office," he said, "but I felt I could do more to help more people working legislatively."

Barrasso, now 54, won the seat and was re-elected in 2006. His greatest accomplishment as a state senator, he said, was co-sponsoring the Hathaway Scholarships program, which gives eligible students scholarship money to attend the University of Wyoming or any state community college. "It was sponsored by two Republicans and two Democrats and ultimately was signed by a Democratic governor and named for Republican governor [Stanley Hathaway]," Barrasso said. "It was the best of bipartisan support for a worthy public policy."

An ongoing desire to broaden the scope of his influence compelled Barrasso to seek the vacant U.S. Senate seat. "I wanted to do on the national level what I had been doing on the state level," he said, "provide quality education for kids, quality jobs for communities and health care accessibility for everyone."

Gary E. Friedlaender, M.D., HS '74, the Wayne O. Southwick Professor and chair of orthopaedics, met Barrasso during his training at Yale and has stayed in touch over the years. What

characterized Barrasso as a resident, he said, was his “strong intellect and highly capable technical skills. As a house officer, he was a great physician who had compassion, commitment and ethical moral character.”

Barrasso says he supports “lower taxes, less spending, traditional family values, local control and a strong national defense.” In the state senate he received an “A” rating from the National Rifle Association, voted for prayer in schools, voted against gay marriage and sponsored legislation to protect the sanctity of life.

“In today’s world, his views would earn him a conservative label,” Friedlaender said, “but John is not inured to the needs of people, especially in terms of health care. I would describe his politics as thoughtful.”

In his new job as a U.S. senator, Barrasso serves on the Senate Energy and Natural Resources Committee, the Environment and Public Works Committee and the Indian Affairs Committee.

The senate seat Barrasso filled doesn’t come up for re-election until 2012, but Barrasso must run as the incumbent in a special election during the 2008 general election.

Friedlaender calls Barrasso’s ability to combine a health care mindset with his political skills a “powerful partnership. He’ll do more with it than the average individual,” he predicted.

—Jennifer Kaylin

## The physiological and the psychological: how women and men are different

**Louann Brizendine**, M.D. ’81, never suspected that her third-year psychiatry rotation would lead to her becoming a best-selling author. Recalling that rotation, she said, “I was stunned by the two-to-one female/male ratio. No one knew why so many patients were suicidally depressed women.”

Over the past 25 years Brizendine, director of the Women’s Mood and Hormone Clinic at the University of California, San Francisco (UCSF), has developed many theories about women’s psychological issues. She finally explained them in *The Female Brain* (Morgan Road Books, 2006), which sold 80,000 copies in its first four months and has been translated into 18 languages. Brizendine believes that physiological differences between men and women lead to significant psychological differences—for example, oxytocin, “the hormone of intimacy,” causes women to crave social contact far more often than men.

Her interest in women’s mental health continued during a psychiatry residency at Harvard and on into her private practice. Recruited by UCSF in 1988, Brizendine taught psychiatry. “Then I got pregnant, and had all the postpartum hormones,” she said. “Phases of a woman’s life were no longer theoretical.”

She began working with UCSF neuroendocrinologists to explore whether fluctuating hormones could trigger women’s mood disorders. “A progesterone metabolite in the brain decreases at menstruation, causing

[symptoms similar to] Valium withdrawal: emotional sensitivity, mood changes, etc.,” observed Brizendine, who had read the literature about hormones, estrogen and neurochemical brain changes in mammals. “Animal models aren’t adequate—you can’t ask a mouse how its mood is today.”

Her new perspective led to an innovative course at UCSF in 1993, “Hormones in Psychiatry,” which quickly evolved into her mood and hormone clinic. The clinic now treats about 600 women annually.

Brizendine’s research into hormones led her to a startling conclusion. “It hit me like a lightning bolt—testosterone causes sexual desire. No one ever thought the problem of frigidity might be biological! I started measuring testosterone and correlating it with sexual interest in females. Levels were often low. Watching patients suffer, knowing other psychiatrists weren’t seeing it the same way, I felt a passion to clarify biological aspects of women’s mental health and hormonal issues,” she said.

Surprisingly, some patients wanted to stay on the antidepressant Prozac, even though one of its side effects is decreased libido. They were choosing better moods over better sex. In early Prozac trials, manufacturer Eli Lilly and Company had found (but not publicized) women’s orgasmic difficulties. “Female sexual problems are treated as just ho-hum,” Brizendine said, “but erection or ejaculation problems are treated as a medical emergency.”

Her book’s provocative claims—including the contention that oxytocin gives females so much pleasure that they crave connections like gossip with friends to get that “rush”—are criticized



ANDY FREEBERG

Louann Brizendine believes that psychological differences between men and women have their roots in physiological differences. Throughout her career she has explored the biological aspects of women's mental health.

for exaggerating gender differences or oversimplifying research. Some social scientists say her unflattering, dubious presentation of female behaviors weakens crusades for equal pay and opportunities.

Other colleagues remain unruffled. Bruce McEwen, PH.D., head of the Harold and Margaret Milliken Hatch Laboratory of Neuroendocrinology at Rockefeller University, confirmed the biological basis of sex differences in brain and behavior. "Sex hormones and experiences interact over the entire lifespan and alter brain structure and function in both men and women. Brizendine perhaps has not emphasized [these ongoing interactions] as much as she might have."

He appreciates Brizendine's efforts to "elucidate biological bases of how many men and women behave. Whether she's contributed to more prejudice, in spite of the best intentions to educate ... is to me the almost inevitable price of writing about this topic."

Brizendine, ruefully aware of the controversies, had aimed to preclude them. In a mass-market book, she discovered, "you can't go into details of how and where a study was done. I wrote a more sophisticated section for people in science, so that anyone wanting to know more could go to those 45 pages of notes at the back." However, determined to shorten the length of *The Female Brain*, the publisher deleted all of Brizendine's painstaking explanatory notes during final editing.

How does she endure the negative reactions? "I just breathe deeply," Brizendine said. "Some days, I need ovaries of steel."

—Carol Milano

## Policy expert finds answers to large health problems come from diverse teams

In the 30 years that **Darryl E. Crompton**, J.D., M.P.H. '76, has worked as a public health lawyer, nothing prepared him for the moment he held a 4-month-old South African girl dying of AIDS. As she wheezed and shivered in his arms, all he could think about was how governments, nonprofit organizations and religious groups had failed her and the nearly 1 million other AIDS orphans in Africa.

"This was the first time I had held someone who was dying," Crompton said. "It made me more sensitive and committed to make a contribution to social change related to AIDS and poverty."

Crompton spent a month in South Africa in 2005 as a consultant for the humanitarian organization CHF International. His assignment was to determine how well the country's social infrastructure supports AIDS orphans, some of whom have AIDS themselves.

South Africa was one of many stops on a professional journey dedicated to improving the health of the poor and uninsured, especially children. Crompton, who received his law degree from the University of California, Davis, and his master's degree in public health from Yale, has taught health law, policy and bioethics at the University of Alabama; trained Siberian physicians in health care policy; and studied pediatric patients' rights in Scotland, England and Denmark. He is now director of the Institute for International Public Policy of the United Negro College Fund Special Programs Corporation in

Washington, D.C. He is also a lawyer and policy, management and organization development consultant in Washington.

Crompton became sensitized to the plight of the poor as a boy. His parents wanted their children to have a multicultural education, so when Crompton was 11, the family left their home in Los Angeles to spend a year in Morocco. “I saw other 11-year-old children who had dropped out of school and were working in various and sundry jobs,” he said. “People were living in mud huts with no running water.”

Crompton’s father worked as an architect, a profession that provided the family with opportunities for international travel. Their next move was to Copenhagen, where Crompton experienced socialized medicine for the first time. When he or members of his family got sick, they received high-quality health care—for free.

Growing up in the political crucible of the civil rights movement and the Vietnam War, Crompton knew he wanted to contribute to social change. He considered becoming a dentist because of his interest in science, but instead chose a career in public health and health policy. “When I looked at how I could make a contribution to social change in health, it wasn’t through the practice of medicine, one patient at a time, but through public policy,” he said.

After graduating from the University of California, Los Angeles, he decided to study law. As a law student Crompton took courses in public health. Those classes, combined with an internship in the Washington office of U.S. Rep. Yvonne Braithwaite Burke, a Democrat

from Los Angeles, convinced him to work for an M.P.H. as well.

At Yale, Crompton was pleasantly surprised by the varied backgrounds of his classmates. “We had teachers, musicians, nuns, priests, mathematicians, people with philosophy backgrounds. It was very exciting for me.”

In fact, that multifaceted learning environment informs his approach to public health to this day. “I don’t have a magic bullet, but I know the only way you can achieve transformational change is through interdisciplinary teams of people.” He notes that if a patient with HIV or AIDS is homeless or can’t afford food, antiretroviral drugs alone aren’t going to offer much help.

Crompton saw the complexity of health issues when he was hired in 1988 by the Florida commissioner of education to evaluate drug prevention programs for adolescents. “There are lots of drug and alcohol prevention models, but basically very few are effective,” he said. “It’s an example of the interconnection between public health care and a whole range of broader social, political and cultural issues.”

Crompton is also interested in diversity of another sort. There should be more diversity and minority representation in health care, he says. He would like medical and public health schools, such as Yale’s, to identify, nurture and support talented minority middle and high school students to prepare them for careers in public health.

It’s all part of his lifelong goal of providing universal access to health care. “I don’t see a lot of caring in the health care system,” he said. “How can we improve the caring part of health care?”

—Lori Ann Brass



TOM RADCLIFFE

**Darryl Crompton first thought of becoming a dentist, but chose public health policy as a career in order to contribute to social change. His ultimate goal is to see universal access to health care.**

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### **Familiar Faces**

**Do you have a colleague who is making a difference in medicine or public health or has followed an unusual path since leaving Yale? We’d like to hear about alumni of the School of Medicine, School of Public Health, Physician Associate Program and the medical school’s doctoral, fellowship and residency programs. Drop us a line at [ymm@yale.edu](mailto:ymm@yale.edu) or write to Faces, *Yale Medicine*, 300 George Street, Suite 773, New Haven, CT 06511.**



HAROLD SHAPIRO

## Alumnus receives Yale Medal

A typical Thursday morning usually finds Samuel D. Kushlan, M.D. '35, HS '37, attending morning report, reading journal articles in the library and going to internal medicine grand rounds. Retired since 1982, Kushlan, now 95, still drives almost every day to the hospital where he has worked for 70 years and continues to be a role model for younger colleagues.

Kushlan has received many honors throughout his distinguished career. In November he received the 2007 Yale Medal in recognition for his years of leadership. The medal, the highest award bestowed by the Association of Yale Alumni, is given annually to five alumni in honor of outstanding service to the medical school and the university.

Born in New Britain, Conn., in 1912, Kushlan was so inspired by his local doctor that by the age of 10 he knew he wanted to be a physician. After graduating from the School of Medicine, he completed his residency at what was then New Haven Hospital, earning a salary of \$25 a month. "Medicine was very primitive 70 years ago," he recalled. His main diagnostic tools were taking a medical history and doing a physical exam—X-rays were the only imaging technique available; and in those pre-penicillin days, the principal medications were aspirin, digitalis, phenobarbital, quinine and morphine. Today more than 4,000 medications are listed in the *Physicians' Desk Reference*.

Except for a brief stint at Harvard in 1938, Kushlan spent

his entire career at Yale. He established the first endoscopy clinic in Connecticut in 1942 and was the sole member of the gastroenterology section from 1938 until 1955.

From 1967 until his retirement, Kushlan served as the associate physician-in-chief at Yale-New Haven Hospital and as a clinical professor of medicine. When he retired, one of the hospital's medical services was named for him, although he said he feels out of place among the other legendary physicians—Elisha Atkins, M.D.; John P. Peters, M.D.; Gerald Klatskin, M.D.; Allan Goodyer, M.D.; and Robert Donaldson, M.D.—with whom he shares this honor.

Although he says he does more learning than teaching these days, Kushlan still has some wisdom to impart from the days when the practice of medicine relied more on observation than on diagnostic tests. He advises colleagues to use such simple diagnostic methods as having a patient with back pain lie down to determine its source: if the pain goes away, it's muscular; if it doesn't, it's internal. "I sort of toss in a pearl from time to time to pay my way," he said.

In addition to his activities at the hospital and the lectures and concerts he regularly attends with Ethel, his wife of 73 years, Kushlan also remains an active member of the executive committee of the Association of Yale Alumni in Medicine. "I enjoy the opportunity to be busy," he said.



Rock Positano



Cargill Alleyne Jr.

## 1960s

**Charles R. Rosenfeld, M.D., HS '67**, has stepped down after 30 years as director of the Division of Neonatal-Perinatal Medicine at the University of Texas Southwestern Medical Center in Dallas. He also stepped down as director of the fellowship training program. He will retain his position as the George L. MacGregor Professor of Pediatrics and continue his research on cardiovascular physiology during pregnancy. Rosenfeld is in the 32nd year of an NIH grant to study uroplacental blood flow. "My start in pediatrics and exposure to neonatal care and research at Yale influenced my career choices," he writes.

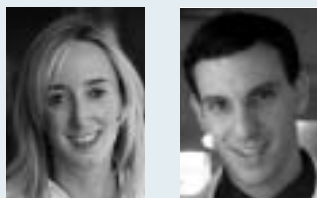
## 1970s

**Steven H. Moffic, M.D. '71**, has begun writing a column, "The Ethical Way," for *Clinical Psychiatry News*, a monthly publication for psychiatry specialists. A professor of psychiatry and behavioral medicine at the Medical College of Wisconsin, he has also written about psychiatric perspectives on global warming.

## 1980s

**Mary Ann Evans, M.P.H. '80**, is working as a substitute teacher in Chicago and Washington, D.C. She has been an active member of the American Public Health Association, participating in the Each One Teach One membership drive.

**Rock G. Positano, D.P.M., M.P.H. '89**, a specialist in foot and ankle health, is writing a health column for *The Huffington Post*. His first columns offered warnings



**Andrea Humphrey Stephen Vindigni**

about the dangers of flip-flops and heavy backpacks for school-children. Positano, who directs the Non-surgical Foot and Ankle Service at the Hospital for Special Surgery in New York City, also writes a health column for the *New York Post*.

## 1990s

**Cargill H. Alleyne Jr., M.D. '91**, associate professor and vice chair for education and research in the Medical College of Georgia (MCG) Department of Neurosurgery, was named the Marshall Allen Distinguished Chair of the department in September. Alleyne went to MCG in 2004 from the University of Rochester Medical Center, where he was chief of the Division of Stroke and Cerebrovascular Neurosurgery and associate residency program director for the Department of Neurological Surgery. At MCG he directs the Neurosurgery Vascular Service and the Neurosurgery Residency Training Program and co-directs the Cerebrovascular Research Laboratory.

**Melissa T. Berhow, PH.D. '96, M.D. '97**, assistant professor of anesthesiology at Stanford University, and Rick Bentley welcomed the arrival of their son, Logan Alaric Bentley, on July 20. Logan weighed in at 9 lbs., 12 oz. Everyone is doing well.

**Brian "Ari" Cole, M.D., M.P.H. '95**, was selected to join the Harvard-Radcliffe Chorus, one of the Holden Choral Ensembles at Harvard. Cole is currently a student at Harvard's Kennedy School of Government, where he recently had the chance to question U.S. Secretary of Health and Human Services

Michael O. Leavitt on the use of steroids in the meat and poultry industry.

**Linda G. Marc, M.P.H. '92**, was married on March 30 to Jean R. Clérismé, PH.D. '96, foreign minister for the Republic of Haiti. Marc is a researcher in the psychiatry department and in the Cornell HIV Clinical Trials Unit at the Weill Medical College of Cornell University. Clérismé, formerly an ambassador from Haiti to international trade organizations, is an authority on economics, development and cultural anthropology.

## 2000s

**Kee Chan, PH.D. '07**, was selected by the National Institutes of Health (NIH) as one of four research participants to attend the 57th Lindau Meeting of Nobel Laureates and Students in Lindau, Germany, in July. Chan conducted research at the NIH while completing her doctorate in public health at Yale. Since 1951, Nobel laureates in chemistry, physics and physiology or medicine have convened annually in Lindau to meet with students and young researchers from around the world. The gathering allows participants, most of whom are students, to benefit from informal interaction with the Nobel Prize winners.

**Bridgid T. Curry, M.P.H. '07, M.E.M. '07**, was married on June 2 to Amos H. Presler in Schuylkill Haven, Pa. In August Curry became a presidential management fellow and regulatory analyst at the Environmental Protection Agency in Washington, D.C. Presler attends law school at American University.

**Andrea C. Humphrey, M.P.H. '05**, was married in July to Jonathan T. Schmidt, J.D. '06, in Minnetonka Beach, Minn. She is a doctoral student in international health and development at the Tulane University School of Public Health and Tropical Medicine in New Orleans and a management consultant in Philadelphia. Her husband is an associate at Ballard Spahr Andrews & Ingersoll, a law firm in Philadelphia.

**Dena J. Springer, M.D. '04**, was married to David E. Novick, J.D., on September 2 in West Hartford, Conn. Springer, who completed her residency at Children's Hospital Boston in June, is a staff physician at Pediatrics of New York. Novick is an assistant district attorney in the trial division and the sex crimes unit of the New York County District Attorney's Office.

**Stephen Vindigni, M.P.H. '04**, has enrolled at Emory University School of Medicine to pursue an M.D. After receiving his public health degree, Vindigni worked for the National Center for Environmental Health of the Centers for Disease Control and Prevention, advancing environmental public health. He traveled frequently to Kenya to work on projects related to safe drinking water and to developing a database to track Kenya's nursing workforce capacity.

## SEND ALUMNI NEWS TO

Claire M. Bessinger, *Yale Medicine*,  
300 George Street, Suite 773,  
New Haven, CT 06511, or via e-mail  
to [claire.bessinger@yale.edu](mailto:claire.bessinger@yale.edu)

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## 2007-2008

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**John W. Berg, M.D.** '51, a pathologist and cancer epidemiologist, died on July 6, at his home in Tempe, Ariz. He was 82. Berg enlisted in the Army after two years at Yale College and then returned to Yale after service in Europe during World War II. He completed his training at Memorial-Sloan Kettering Hospital in New York City in 1955, and then joined the staff as a pathologist/cytologist. He joined the National Cancer Institute in 1965 as a pathologist/epidemiologist. In 1973 he became director of the Iowa State Cancer Registry and professor of preventive medicine at the University of Iowa. In 1977 he moved to Colorado, where he served first as director of epidemiology and statistics at the Comprehensive Cancer Center, then as professor of pathology and preventive medicine at the University of Colorado Health Services Center. He was author or co-author of over 100 research papers and articles, primarily on cancer pathology and epidemiology, and served as editor of *Cancer*, the journal of the American Cancer Society.

**Richard W. Breck, M.D.** '45, died on July 30 at his home in Wallingford, Conn. He was 89. Breck served in the U.S. Army during World War II and was a medical officer at Scott Air Force Base, Fort Belvoir and Walter Reed General Hospital. He was an attending physician at Meriden-Wallingford Hospital from 1949 to 1981 and chief of staff at the hospital from 1960 to 1962. He also served as medical director and attending physician for the former Convalescent Home, now the Regency House of Wallingford;

from 1949 to 1980 he was physician for the International Silver Company. A former secretary of the executive committee of the Association of Yale Alumni in Medicine, he received the Distinguished Alumnus Award in 1988. Breck retired from general practice in 1995 but continued to see geriatric patients on a part-time basis.

**Robert C. Charman, M.D., FW '64, HS '67**, died on May 8 at his home in Lebanon, N.H. He was 71. In 1967 Charman joined the staff at Mary Hitchcock Memorial Hospital in Lebanon and served in various positions, including acting chair of medicine, director of clinical services for the Department of Medicine and director of the office of graduate and continuing medical education. In 1992 he published *At Risk: Can the Doctor-Patient Relationship Survive in a High-Tech World?* The book, written for patients and their families rather than physicians, was favorably reviewed by the *Annals of Internal Medicine* in 1993. Charman served as vice president of the New Hampshire Medical Board and chair of its Medical Review Subcommittee until 1996.

**Kenneth M. Frankel, M.D., HS '66**, died of cancer on June 17 at his home in Longmeadow, Mass. He was 66. After an internship at Yale, Frankel served in the U.S. Army Medical Corps in Vietnam from 1967 to 1969. For his service he received several medals, including the Bronze Star. He was one of the founding members of Vietnam Veterans Against the War. In 1974 he moved to Longmeadow, where he was chief of thoracic surgery

at Baystate Medical Center in Springfield. He taught at Tufts University School of Medicine and published a number of articles on pulmonary malignancies, self-inflicted chest wounds and the management of dyspnea.

**Laurie B. Hickey, M.D. '00, M.P.H. '00**, died on May 24 in Ithaca, N.Y. She was 36. While at medical school, Hickey traveled to Gabon, Africa, to work at the Albert Schweitzer Hospital in Lambaréné. Upon her graduation she completed a residency in pediatrics at Children's Hospital Boston and Boston Medical Center. She moved to Auburn, N.Y., in 2005, where she joined the Auburn Pediatrics Group as a primary care pediatrician. Hickey was a candidate fellow of the American Academy of Pediatrics.

**Russell Miller Jr., M.D. '55, PH.D.**, died on June 18 in Elk Grove, Calif. He was 80. Miller practiced medicine in the East Bay area for more than 30 years and was an associate clinical professor at the school of medicine of the University of California, Davis.

**Monica A. O'Neill, M.P.H. '86**, died on August 18 of cancer at her home in New Haven. She was 49. Until her illness O'Neill was a senior vice president of the PMA Insurance Group of Pennsylvania.

**Sidney N. Paly, M.D. '52, FW '54, HS '58**, died in Marblehead, Mass., on September 23 after a brief illness. He was 81. Paly, born in Brooklyn, N.Y., to Russian and Polish immigrants, graduated from Stuyvesant High School for Science in 1943 and spent the war years in the Army Specialized Training Program.

Following the war he graduated from Clark University in 1948. He completed neurosurgical fellowships in Sweden and London. In 1959 he joined the North Shore Medical Center in Massachusetts as one of Salem Hospital's first two neurosurgeons. He served as chief of neurosurgery from 1966 until 1989 and practiced at Salem and Beverly hospitals until his retirement in 2006. That year he was honored by the Essex South District of the Massachusetts Medical Society as a Community Clinician of the Year. Paly served as president of Cohen-Hillel Academy from 1972 to 1973. He also was a recipient of the Dr. E. Augustus Holyoke Memorial Award in 2002, which recognizes professional excellence and service to the community.

**Morton F. Reiser, M.D.**, the Albert E. Kent Professor Emeritus of Psychiatry and training analyst at the Western New England Psychoanalytic Institute, died on June 21. He was 87. Reiser served in the U.S. Army during the Korean War and was a research psychiatrist at the Walter Reed Army Medical Center. He joined the faculty of the Albert Einstein School of Medicine, trained at the New York Psychoanalytic Institute and joined the faculty there. In 1969, Reiser came to Yale, where he was the Charles B.G. Murphy Professor and chair of psychiatry until 1986. Reiser's leadership fostered the emergence of the Connecticut Mental Health Center and of the psychiatry department as a preeminent psychiatric program. He advanced an approach to psychiatric illness that linked biological, psychological and social dimensions of illness. He also probed the interface of the psy-



chology and biology of consciousness, particularly altered states of consciousness.

**Thomas R. Shea, M.D.** '58, died on July 21 at his home in Sherman, Texas. He was 75. After graduation Shea was an intern in general surgery at Philadelphia General Hospital and completed his residency in eye surgery at Parkland Memorial Hospital in Dallas. He subsequently settled in Sherman because he felt the city needed an eye surgeon with his training and experience. He served the community as an ophthalmologist for more than 40 years.

**Rajinder S. Sikand, M.D.**, a former assistant professor of medicine and a physician at Yale University Health Services, died on July 23 in Southbury, Conn. He was 83. Sikand was a graduate of the University of the Punjab Medical School in Lahore, Pakistan, and completed his clinical training in the United States and England. His interest in pulmonary physiology led to the publication of several articles on electrocardiography at Yale in the 1940s and 1950s and to a position as visiting scientist at the Max Planck Institute for Medical Research in Heidelberg, Germany, in 1964 and 1965. In 1967 Sikand returned to the United States to serve as a lecturer and researcher at the State University of New York at Buffalo. After 1969, he focused his efforts on research and teaching at Yale and was a physician at Yale-New Haven Hospital. In 1973, Sikand was hired as a physician at Yale University Health Services. In 1975 he joined the Hospital of Saint Raphael in New Haven as co-director of the Pulmonary

Section. After retiring to Southbury in 1993, Sikand read extensively about art, philosophy and history and nurtured a late-life infatuation with golf.

**Nicholas P.R. Spinelli, M.D.** '44, a much-loved physician and medical educator, died on November 30, 2007, in Milford, Conn. He was 86. The son of immigrants from Italy, Spinelli entered Yale College in 1937 and started medical school in 1941. During World War II, he served in the U. S. Army as a neuropsychiatrist in Germany. His medical career of more than six decades included nearly 20 years of community service as an internist in Stratford, Conn. He subsequently became director of medical education at Bridgeport Hospital, where he developed a collaboration with the Yale School of Medicine that included a program in pediatric medicine and recruitment and training of medical practitioners and educators from developing countries. Today scores of practicing physicians credit their careers to his training and mentorship. Spinelli retired from Bridgeport Hospital in 1985 and became director of alumni affairs at the School of Medicine. One of his primary interests was the well-being of students, and early on he recognized the importance of scholarship aid. He helped to establish the Class of 1944 Scholarship Fund, which supports three students each academic year. He remained devoted to his classmates, keeping them in touch over seven decades. Spinelli received numerous awards for his service to Yale, including the Distinguished Alumni Service Award, the Peter Parker Medal and Yale's highest alumni honor,

the Yale Medal. Of all the honors, he would say, the most important came when he was 16 years old. "The greatest gift I got was the letter saying I was accepted to Yale."

**Lee Van Lenten, M.D.** '66, died on September 11 in Rockville, Md., after a brief illness. He was 69. Van Lenten retired in 1995 after 24 years at the National Institutes of Health (NIH), where he served as a health science administrator at the National Institute of Medical Sciences. In the mid-1980s Van Lenten was the administrator of the NIH's Medical Scientist Training Program, which supported M.D./PH.D. candidates. He administered a portfolio of grants in the areas of physiology, trauma and burn injuries. He also published several articles on the radioactive labeling and chemical modification of glycoproteins. Van Lenten received two Commendation Medals and an Outstanding Service Medal during his years at the NIH.

**Walter A. Van Sandt, M.P.H.** '52, died on August 30 in Oakland, Calif. He was 89. During his career Van Sandt was an industrial health and safety engineer, publishing articles on the safety design of welders' helmets, beryllium spectrographs and the calibration of mercury vapor detectors.

**M. Henry Williams Jr., M.D.** '47, died on September 16 in Berlin, Vt. He was 83. Born in New Haven, Williams was a '45W graduate of Yale College. He completed his internship and residency at Columbia University. During the Korean War Williams

was a captain in the U.S. Army and chief of the respiratory section at Walter Reed Army Medical Center. He was a professor of medicine and director of the division of pulmonary medicine at Albert Einstein College of Medicine in New York from 1958 until his retirement, and also served as director of the Chest Service at the Bronx Municipal Hospital Center. Between 1972 and 1976, he was chair of the advisory committee of the Yale Lung Research Center. He was managing editor of *Lung* for many years and served on the editorial boards of *Pulmonary Perspectives*, *Excerpta Medica*, and *Respiratory Times*. He retired from Albert Einstein in 1994 and received emeritus status in 1998.

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**SEND OBITUARY NOTICES TO**

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JOHN CURTIS

## Five years later, adjusting to the 80-hour week

In July 2003, when the national council overseeing medical education limited residents' work hours to no more than 80 per week, medical school faculty and hospital staff around the country saw the intervention as a mixed blessing [See "Recreating the Residency," Fall/Winter 2004]. On the one hand, the Accreditation Council for Graduate Medical Education was responding to public fears that overworked residents might make poor medical decisions; on the other hand, fewer hours on duty carry the risk of less continuity of care.

At the School of Medicine, balancing these two concerns has called for flexibility. "We've had to adapt continually, and we're still adapting," said Rosemarie L. Fisher, M.D., HS '75, associate dean for graduate medical education. Peter N. Herbert, M.D. '67, chief of staff and senior vice president for medical affairs at Yale-New Haven Hospital, acknowledged that sticking to an 80-hour week has been difficult for some programs, particularly those in intensive care units. The hospital has redistributed the workload by taking on more physician assistants and advanced-practice registered nurses. Still, some faculty and administrators worry that residents may feel obliged to do as much work as before—as much consulting with patients, analyzing as many lab results—in fewer hours. Fisher looks to further fine-tuning of the regulations—for instance, pilot programs that incorporate a mandated rest period—to address this potential problem.

In response to the new work rules, some specialties have created more positions for residents: neurosurgery, for example, has expanded from six residency positions to 12. Even in the midst of a long in-hospital shift, evidence of the new rulings is apparent. Areas have been set aside for residents to rest undisturbed, and such arrangements have "probably worked out better for everyone" than the marathon-like conditions that prevailed earlier, said Herbert. "I think the system as a whole has acclimated very well."

—Sandra J. Ackerman

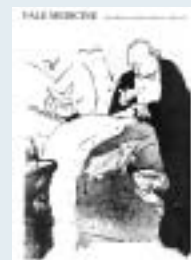


## Medical School Building Demolished

—*Alumni Bulletin*  
January 1958

"About 1860 the Yale School of Medicine moved from the old South Sheffield Hall to a private dwelling at 150 York Street. The school quickly outgrew the facilities offered by these premises, and about 1890 an additional structure was erected in the rear of the building. As the growth of the school continues, new facilities were acquired, including the Anthony N. Brady Memorial Laboratory (1917), and the original building was used entirely for anatomy.

"The building at 150 York Street was occupied by the school until 1922 and will be remembered by many alumni as the original medical school building. Although it was no longer a part of the school, the building continued to stand until December of 1957, when it was demolished as part of the city's Oak Street Redevelopment Project."



## School's Building Projects Earn Recognition

—*Yale Medicine*  
Spring 1983

"Two recent School of Medicine building projects have received awards. The New Haven Preservation Trust presented a Merit Award to the School for its sensitive rehabilitation and creative reuse of the historic Jane Ellen Hope Building. The oldest building on the School's campus, the red brick and rough stone building was built in 1902 as a clinic building. Renovations by architects Alexander Purves and Allan Dehar Associates for its use as a teaching facility were completed last fall.

"First prize for excellence in consulting engineering in the category of mechanical and electrical design was awarded the School by the New York Association of Consulting Engineers for fostering excellence in engineering of its new chilled water thermal storage system. The firm of Meyer, Strong and Jones, P.C., were mechanical and electrical engineers for the facility, which was built to increase the capacity of the Sterling Power Plant in order to provide air conditioning for the Yale-New Haven Medical Center.

"Augustus G. Kellogg, director of facilities planning for the School, was responsible for organization and planning of both projects."

## WEST CAMPUS NOW PART OF YALE

With the \$109 million purchase in September of what is now known as the university's West Campus, Provost Andrew D. Hamilton, PH.D., is asking faculty and other leaders on campus for their ideas on the best use of the property—the 136-acre former Bayer HealthCare complex that straddles the neighboring towns of West Haven and Orange. Its 17 buildings have 1.5 million square feet of space for laboratories, offices and storage. In comparison, the medical school campus occupies 2.5 million square feet.

“There will be a focus on a number of different areas for planning,” Hamilton said. “The first, of course, is science. The number one priority for the university at West Campus is the opportunity that it gives us to do things in biomedical science that we have not been able to do for lack of space.”

Other ideas under consideration include using the space for storage; displays of collections belonging to university museums, galleries and libraries; and outreach programs to local schools.

“Planning is for the long-term integration of the West Campus into the life—scholarly, scientific and medical—of Yale University,” Hamilton said. “It is not going to be an overflow campus. It is not going to be a place where we put things that don't fit at the university.”

—*John Curtis*



ROBERT LISAK (2)



Yale's new West Campus includes 550,000 square feet of laboratory space for both biological and chemical research. Medical research is a high priority for use of the new campus.

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