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Fall 2008

Yale Medicine : Alumni Bulletin of the School of Medicine, Autumn 2008- Spring 2009

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A Yale alumna in the rain forest

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autumn 2008

A huge NIH grant boosts bench-to-bedside research, but many scientists still want to follow their noses



Valie mediane

AUTUMN 2008

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We should expect our students to be literate

It was with some sadness that I read of the teaching of ethics by my colleague, Alan A. Stone, M.D. '55, to his students at Harvard Law School. ["A Passport to the Young," Yale Medicine, Spring 2008] Stone felt obliged to turn to the movies because "few students had read Sophocles or Dostoevsky, Austen or Flaubert." I was reminded of how startled I was some years ago to discover that one of my patients, a graduate student in literature at Yale and a magna cum laude graduate of Yale College, had never read a work by Shakespeare.

Should our top law and medical schools be admitting people who haven't even a rudimentary reading knowledge of the Western canon? Perhaps what is needed is not a "new passport to the young," but a reactivation of the old one. And perhaps we cannot absolve ourselves of some of the blame for the illiteracy of the young until we make it clear to them that we expect them to be literate.

Victor A. Altshul, м.D. '6о Associate Clinical Professor of Psychiatry

Med school missing from cover

I find an interesting example of the complex relationship between the School of Medicine and the main campus represented by the absence of the topography of the medical campus on the cover of last spring's issue of Yale Medicine. Robert B. Duckrow, M.D. '75, HS '79 Associate Professor of Neurology

and Neurosurgery

vale medicine

Alumni Bulletin of the Yale University School of Medicine Autumn 2008, Volume 43, No. 1

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Yale Medicine is distributed to alumni, faculty, students and friends of the School of Medicine, as well as to leaders in Yale University alumni activities.

Abbreviations commonly used in Yale Medicine include HS to denote the final year of residency for house staff, FW for the final year of a fellowship, EPH for the Department of Epidemiology and Public Health and the School of Public Health and YNHH for Yale-New Haven Hospital.

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starting point

Basic science vs. translational research, and medicine and rain forests

In the autumn of 2006, Yale became one of a handful of medical schools to receive a CTSA grant from the National Institutes of Health (NIH), a boon to translational research here and around the country. Once the program was up and running we asked writer Jill Max to take a look at the new Yale Center for Clinical Investigation, created and funded with the goal of supporting clinical research. This enhanced emphasis on translational research also prompted us to explore the tension between basic-science researchknowledge for knowledge's sake—and the bench-to-bedside goals of those who start out with a cure or treatment in mind. Boston-based science writer Pat McCaffrey talked to scientists at Yale and found that, largely due to a flat NIH budget, scientific research is going through hard times. But some scientists also worry that basic research is taking a back bench to translational research.

More than two years ago, in May 2006, we heard from Kinari Webb, M.D. '02, who asked if we'd be interested in an article about her work in Indonesia. Four years out of medical school, Webb had laid the groundwork to open a clinic in a remote area of Borneo. In addition to her desire to provide medical care to an underserved area, she and her husband, a Harvard ecologist, wanted to link that to preserving the region's rain forests. For more than a year Jill Max has been in contact with Webb, following the progress of the clinic, which opened in the summer of 2007. Her report begins on page 30. 3

John Curtis *Managing Editor*

SECOND OPINION BY SIDNEY HARRIS



"LET'S SEE NOW ... "



The death of Mila Rainof, a month before her graduation, sent a shock throughout the medical school. Her classmates posted her photo and left flowers at the site of the accident.

A student's warm heart and "amazing" smile

Mila Rainof's embrace of others has inspired an enduring memorial at the medical school.

As the 96 members of the Class of 2008 processed to Old Campus for Commencement on May 26, they paused at the corner of York Street and South Frontage Road. One by one, each graduate placed a carnation in memory of Mila Rainof, a classmate who was not with them in the procession.

On April 19 Rainof was struck by a car as she crossed the intersection. She died the next day of her injuries. At a medical school town meeting called by Dean Robert J. Alpern, M.D., on the Monday after Rainof died, Alpern said, "The medical school family has lost a member way too young in age."

In the wake of her death, Rainof's friends and classmates have found many ways to honor her. Her close friends stood by Rainof's parents and sister when they came to New Haven and organized a memorial service in the medical school's Rose Garden. Others began collecting photos and remembrances for a book to be given to her family. Students have organized efforts to improve safety at intersections near the medical school. (See sidebar.) A memorial scholarship and award fund is being established at the School of Medicine to honor and perpetuate Rainof's memory, in particular her compassionate spirit and humanistic approach to medicine. Students also planted a cherry tree in her honor on Harkness Lawn.

Rainof's parents have shared with Merle Waxman, director of the Office for Women in Medicine and a mentor to Rainof, that their daughter loved Yale and was happy here. Her phone calls, they told Waxman, were always filled with her enthusiasm for her classmates, teachers and patients.

What friends remember best about Rainof is her warm and welcoming smile. "Like everyone else," her boyfriend and classmate James Troy said at the Rose Garden memorial, "I was instantly won over by her amazing smile." A friend and classmate, Ellen House, recalled sharing clinical rotations with Rainof and all the patients asking for "the smiley one."

Margaret A. Drickamer, M.D., associate professor of medicine, recounted a trip to Seattle with Rainof to attend a conference. They walked all over the city, she said, talking and telling stories. "We laughed, we cried—and we did go to some poster sessions." Beyond Rainof's warm and friendly demeanor, Drickamer said, was a determination to help people. "Mila really cared about people, especially when she felt a responsibility for their welfare, and she steadfastly refused to let anything get in the way of that caring," Drickamer said.

Karen J. Jubanyik, M.D., assistant professor of surgery (emergency medicine), described a difficult shift at Yale-New Haven Hospital the day after Rainof died. "I just thought, 'What would Mila do?' " Jubanyik said. "She would contribute any way she could. She would go to the patient's side, hold their hand and genuinely listen to them." Friend and classmate Maggie Samuels-Kalow said, "Mila was the person that you wanted at your side when the patient was getting sicker and you didn't know what to do."

Kristina Zdanys, one of the class copresidents, said that the students in the Class of 2008 are a close-knit group and would have felt the loss of any of their members, but that Rainof was special.

After a tragedy, the medical school community mobilizes around traffic safety

On the afternoon of May 22, about two dozen students, faculty and staff from the School of Medicine marched from Cedar Street to the corner of York Street and South Frontage Road, where Mila Rainof, a fourth-year medical student, died after being struck by a car a month earlier.

Pedestrians have long dreaded this and other intersections near the medical school. Drivers in a hurry to reach the Route 34 Connector feeding into Interstate 91 and Interstate 95 routinely run red lights and ignore pedestrian crossing signals.

Students have organized a Traffic Safety Group since Rainof's death their goal is to make the streets safer for pedestrians.

"It is important that we honor Mila and keep the traffic safety effort in the spirit of what she would have done," said Rachel Wattier, a fifth-year medical student who is leading the traffic group. "A lot of people have deep-seated concerns about traffic that they were never able to act on. People see an opportunity to have their concerns addressed." Plans are already under way to improve four intersections adjacent to the medical school area. They are part of a larger plan for street improvements as part of a deal struck between Yale-New Haven Hospital and the city for the construction of the Smilow Cancer Hospital. The model will be the intersection at Cedar Street and Congress Avenue, which has pedestrian crossing lights that flash and count down the seconds remaining for a safe crossing. 5

The hospital will also relocate a truck loading dock at South Frontage Road and York Street under the adjacent Air Rights Garage. Traffic that now leaves the garage onto South Frontage Road will leave through a roundabout to be built where the Route 34 Connector meets the garage.

In light of the planned improvements, the safety group is developing materials to promote pedestrian and cycling safety, petitioning the city government to enforce the city's 25 mile-per-hour speed limit, and calling for strict enforcement of traffic regulations governing stop lights and signs, cell phone use, bicycle lanes and crosswalks.

—J.C.



A few days before Commencement, students, faculty and staff at the medical school rallied at the intersection of York Street and South Frontage Road to urge drivers to respect traffic rules.

—John Curtis

"Whenever she walked into a class or

Marigolds, she was always smiling or

had something nice to say," Zdanys said.

person in the class who always made

people feel good ... she would be the

first person," said Rachel Wattier, who

has been leading a committee that has

met with city and university officials to

students, faculty and others gathered

at the intersection where the accident

occurred. Bearing signs that read "Yield

4 Walkers," and "No Turn on Red," the

group asked drivers to slow down and

Gregory L. Larkin, M.D., professor of

surgery (emergency medicine), said at a

meeting in The Anlyan Center the day

after Rainof died. Larkin had been the

attending in the emergency room when

an ambulance delivered Rainof. The day before the accident, Larkin had been her teacher, instructing her in the use of

ultrasound. Rainof was scheduled to

begin a residency in emergency medi-

cine in Oakland, Calif., after graduation.

away from the curb and safety. She died

the next day of severe head injuries.

On the morning of April 19 Rainof was on her way back to her York Street apartment after working out in the gym in Harkness Dormitory. A truck was leaving the loading dock of Yale-New Haven Hospital against a red light. As Rainof crossed South Frontage Road, also against the red light, the truck cleared the intersection and cars in the three oncoming lanes moved forward. Two swerved to avoid her, but a third struck her when she was just a yard

"There was really no one to blame,"

A few days before Commencement,

improve traffic safety.

respect the traffic lights.

"If you asked people to think of a

School of Medicine goes green as it aims for lower carbon emissions by 2020

The Yale School of Medicine's sustainability campaign is ambitious and costs a little extra, but it's perfectly willing to accept hand-me-down jeans—in fact, that's part of the point.

Denim discarded in the jean manufacturing process, which now helps insulate the Sterling Hall of Medicine's C wing, is one of many recycled materials that are lightening the university's carbon footprint. The building's recently renovated lab casework, ceiling tiles and wall insulation also come from such recycled materials as wheat straw board and soy-based spray foam. In total, the sustainability campaign squeezes more light from the sun, diverts trash from landfills and conserves water and heat.

Adding such features to previously planned renovations costs morebetween 1 and 2 percent of the \$8.2 million price tag of the Sterling renovations that were completed in 2006but Yale can't afford not to do it, said Virginia Chapman, director of construction and renovation for the School of Medicine's facilities office. "We're saving the university money as a by-product of reducing carbon emissions," she said. Still to come, Chapman added, are renovations to the second and third floors of Sterling's I wing, the Brady Memorial Laboratory, the Hunter Building, the sixth and seventh floors of the Laboratory for Epidemiology and Public Health and the Laboratory for Surgery, Obstetrics and Gynecology, all of which will incorporate green features.

Yale's overall sustainability strategy began with the student-initiated



"Yale Green Plan" in 1998. In 2002, the university's Advisory Committee on Environmental Management proposed a set of environmental principles, and in 2005 President Richard C. Levin committed the university to reducing greenhouse gases to 10 percent below 1990 levels by the year 2020.

Implementing a sustainable laboratory renovation that could be benchmarked and measured by a national standard would not come easily. Success is measured by the U.S. Green Building Council's Leadership in Energy and Environmental Design (LEED), but the organization had not set standards for lab renovations. "LEED was designed for new buildings or full-building renovations but not laboratories nor smallerscale renovations of the kind we do here at the medical school," Chapman said.

The work on the third floor of the C wing created a yardstick in 2006 when it became the first laboratory renovation project in the United States to gain LEED gold certification for its sustainable features. Among those features, said Robert Skolozdra, an associate at the architectural firm Svigals & Partners, which designed the renovations, are sensors that switch lights on only when a person is in the room. "Daylight harvesting"-adding windows-maximizes available light. The project eased the strain on landfills by recycling 85 percent of construction and demolition debris. Lab faucets have reduced their output from 2 to 1.5 gallons per minute, and low-flush toilets and urinals have been installed. Water use is now down 35 percent overall.

As green renovations continue at the medical school, officials know that the older buildings will pose a challenge, but The Anlyan Center, which opened in 2003, is also "a big energy user," Chapman said. When it was designed, "other concerns outweighed concerns for the environment." The building is undergoing an energy audit to determine how to address the high energy use, she said.

—John Dillon

New financial aid policy geared toward middle-income families and students

Some students opening acceptance letters from the School of Medicine this spring had another reason to celebrate. While their colleagues in the Class of 2008 graduated with an average debt of \$115,000, a new financial aid formula should ease that burden for middleincome families.

Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, announced the new policy in April. Formerly, parents with a combined income over \$45,000 were expected to help pay the costs of their child's medical education. Beginning this academic year, that threshold has been raised to \$100,000. The "base loan" (the amount students are expected to borrow before receiving scholarship funds) has been raised from \$17,000 to \$18,000, keeping it among the lowest in the country. The new formula applies to all current students.

"What we were expecting was not realistic," said Richard Belitsky, M.D., the Harold W. Jockers Associate Professor of Medical Education and deputy dean for education.

The change was made possible after Yale's endowment income added \$1.1 million to the medical school's financial aid budget. The school's financial aid committee then decided that students from middle-income families needed the extra funds most. Especially needy families did not need to borrow more than the base loan, as School of Medicine scholarships make up the difference, while affluent families were less burdened by tuition costs. The resources of students from middleincome families, though, consistently fell short of the old financial aid formula's estimate, and these students were forced to borrow above the base loan to pay what the school required.

"They should have been borrowing \$68,000—four times the unit loan but the average debt was \$115,000," said Alpern.



Another reason for the change, said Belitsky, was that high debt often influences specialty choice. For example, primary care physicians are in critically short supply nationwide, perhaps in part because they are less well reimbursed than their colleagues in some specialties. Of the 97 Yale students who matched this year, only four entered primary care, and another three entered family medicine. The American Medical Student Association has stated that the current American model of financing medical education harms efforts to improve physician diversity and patients' access to care.

Richard Silverman, director of admissions, speculates that the change may also affect the diversity of the applicant pool. "If another school is widely perceived to be generous or liberal in its financial aid policy, it might get more applications from candidates who assume that Yale, because of the name, is only for the wealthy," he said. Tuition, fees and expenses at the School of Medicine this year are expected to range from \$62,000 to \$69,000.

Other medical schools are also changing their financial aid policies. In March, citing concerns about debt and specialty choice, Harvard Medical School raised its parental-income threshold to \$120,000.

"If a student wants to be a neurosurgeon instead of going into primary care," said Alpern, "I'd hate for them to do it just because of the loans they had." —Jenny Blair

Online: Yale Netcasts

Richard Belitsky: A Great Doctor Is Not What You Know but Who You Are.

et cetera ...

7

PROVOST LEAVES FOR OXFORD

Provost Andrew Hamilton, PH.D., is leaving Yale after 11 years to become the next vice chancellor of the University of Oxford in England.

"As a noted scientist, a successful department chair, university citizen and provost these past four years, Andy has had a remarkable impact on Yale since joining our faculty in 1997," said President Richard C. Levin.

Hamilton helped create the Yale Center for Genomics and Proteomics and the Yale Institute for Nanoscience and Quantum Engineering. He has been instrumental in developing plans for research programs and core facilities for Yale's new West Campus. Hamilton also helped to create the new interdisciplinary Humanities Program and has supported Yale's investments in the arts.

After joining Yale, Hamilton became chair of the chemistry department in 1999. He became deputy provost for science and technology in 2003 and provost in 2004 after then-Provost Susan Hockfield, PH.D., was appointed president of MIT.

In September, Peter Salovey, PH.D., dean of Yale College was named provost. —John Curtis

62 YMG MEMBERS IN TOP DOCS LIST

New York Magazine's 2008 list of the region's top physicians includes 62 physicians from Yale Medical Group (YMG). Yale's "top docs" are in 40 specialties and serve patients of all ages.

The list, which appeared in the magazine's June 16 issue, is based on the *Top Doctors New York Metro Area* guidebook, published annually by Castle Connolly Medical Ltd. The publishers ask doctors throughout the region which of their colleagues they would recommend to a friend or relative. The guidebook includes the top 10 percent of the metro area's physicians. New York Magazine publishes a shorter list—the top quarter of the top 10 percent.

"Our strong representation in the New York metro area highlights the fact that YMG is a regional and, in some cases, national practice," said David J. Leffell, M.D., CEO of YMG. "Patients throughout New York and New England are coming to see YMG as a medical destination of choice."

—J.C.

A stroke of luck saves New London patient

A new telemedicine initiative brought a potentially lifesaving drug to a patient 50 miles away.

When Jeanne Munnelly went for a swim at a high school in East Lyme one August morning, she could not have known she was about to have a stroke—and make medical history in Connecticut.

At about 8:15, as she swam in the school's pool, Munnelly became weak on her right side and unable to speak. Lifeguards pulled her out and emergency personnel based at the fire station across the street arrived within five minutes. She reached New London's Lawrence and Memorial Hospital in just 15 minutes.

That's when Munnelly, 67, became the first patient to benefit from the Yale-New Haven TeleStroke Network, a program modeled on a similar initiative at Massachusetts General Hospital. The TeleStroke Network allows area hospitals to call upon Yale neurologists' expertise in assessing stroke victims. Using high-speed network videoconferencing and image-sharing technology, neurologist Joseph Schindler, м.р., evaluated Munnelly via computer from Yale-New Haven Hospital (УNHH), then gave the "green light" to physicians in New London to use the clot-busting drug tissue plasminogen activator (tPA). Munnelly received the drug only 37 minutes after reaching the hospitalmuch more quickly than if she had been transported to YNHH first.

Schindler said the process of evaluating a stroke patient via TeleStroke is the same as when he sees a patient in YNHH's emergency department. "It's no different; it's just the use of technology to do it remotely," he said.

Speed and decisiveness are critically important in treating stroke victims. Most blood clots that cause ischemic strokes can be dissolved by tPA, a thrombolytic agent. But this medication can also cause bleeding in the brain, and that risk increases beyond three hours after the onset of symptoms. To meet that three-hour deadline and try to prevent this complication, doctors must ensure that a patient is an appropriate candidate for tPA. Yet in most hospitals, neurologists are not always available to assist emergency physicians with the evaluation and treatment decision. As a result, many patients who might benefit from tPA do not receive it.

With telemedical technology, a neurologist need not be physically present. While seated at a computer 50

miles away from the patient, Schindler, the clinical director of the Yale-New Haven Stroke Center, used a high-speed Internet connection to speak with the patient, family and clinical staff and review Munnelly's medical history, blood tests and CT scan. He also examined her using a camera with a zoom feature. She was, he determined, a good candidate to receive tPA. Shortly after receiving the drug, Munnelly regained the use of her right leg as well as some ability to speak.

Schindler, who is optimistic that Munnelly's condition will continue to improve, was pleased not only that the technology worked but also that he and the team in New London could act so quickly. "We've done it at Yale when the entire team was already in the ED; we [assessed and treated the patient] in a similar time. But to have that done remotely, it's wonderful." (See related story, page 9.)

—Jenny Blair



From a console in New Haven, neurologist Joseph Schindler evaluated a stroke patient 50 miles away in New London.

8

With virtual lives on the line, simulations help responders assess triage systems

Imagine being the first paramedic on the scene after a tanker truck has plowed into a city bus. Traffic is snarled, cars are honking and people are screaming. Who needs your attention most the man on the concrete holding his bloodied knee or the woman on her back with closed eyes? What about the people inside the overturned bus? And what is that white vapor drifting from the truck's tank?

In emergencies, prioritizing care for victims is called triage. The word comes from the French *trier*, "to select" or "to sift," a usage that goes back to Dominique Larrey, the chief surgeon of Napoleon's armies. A victim might be color-coded as red, meaning he needs help immediately; yellow, meaning he will need help soon; green, meaning he has minor injuries; or black, meaning he cannot be helped with available resources. But sorting human lives in this way is still more art than science.

This uncertainty persists because, although many rules exist to help rescuers, it is hard to evaluate whether those rules actually save lives. The decades-old Simple Triage and Rapid Treatment (START) system color-codes patients as described above. But like other such systems, said David C. Cone, M.D., associate professor of surgery (emergency medicine) and of epidemiology, "we have no idea if it works."

Cone has spent his career thinking about disasters and mass-casualty triage. He studies emergency medical services and plans for chemical, biological and nuclear terrorist incidents. He has run disaster simulations at Tweed-New Haven Airport complete with volunteers smeared with fake blood. But triage research is inherently difficult. For one thing, said Cone, "we don't even know what we want a mass-casualty triage system to do." Is the best system the one that's easiest to teach? Quickest to apply? Is the most important goal to get patients into ambulances as quickly as possible? Or to save the greatest number of lives? The complexities mount when one considers that every disaster is unique—it is almost impossible to compare triage systems in the real world. Now, though, Cone has begun working with a new tool to study START and other triage systems: a virtual-reality (VR) simulator.

While studying in Italy for a master's degree in disaster management in 2004, Cone saw a VR simulator used to train Dutch firefighters and realized that the software could be adapted for triage research. Developed by the Dutch company E-Semble, the simulator looks like the highly realistic video game Grand Theft Auto. Learners at a laptop "walk around" a vivid scene, assessing and triaging victims. Dangers and distractions, like toxic spills or television reporters, can be added to the scenario. The learners are timed and their actions exported into a database that can then be analyzed.

Working with emergency medicine resident John Serra, м.D., and supported by the Centers for Disease Control and Prevention and the Laerdal Foundation, Cone plans to teach paramedic students two different triage systems several months apart, then compare how they did with each system in identical VR scenarios. "Once we get the software tuned, then we can design the larger studies," said Cone. He plans eventually to use the tool to explore whether rules for triage are even necessary, or whether victims are better off being triaged by experienced rescuers who rely on clinical gestalt.

VR may one day allow researchers around the world to collaborate, exchange scenarios and compile "libraries" of standardized victims. Cone hopes the controlled VR environment will allow for real progress in triage research and ultimately save more lives during real disasters.

—J.B.

et retera ---

CHOCOLATE AND PRE-ECLAMPSIA

Eating chocolate may lower the risk of preeclampsia, a dangerous condition in pregnancy characterized by increased blood pressure and proteinuria, according to a Yale study published in the journal *Epidemiology* in May. But the study is not a free pass for chocoholics. Eating too many sweets can cause health problems, said Elizabeth W. Triche, PH.D., of the Yale Center for Perinatal, Pediatric and Environmental Epidemiology, who led the study.

Triche's team wanted to find out whether chocolate—especially dark chocolate with antioxidants that confer cardiovascular benefits—would protect pregnant women against pre-eclampsia. The study found that women who had more than five servings a week had a lower risk of pre-eclampsia; those who had high levels of theobromine, a byproduct of chocolate consumption, were nearly 70 percent less likely to develop preeclampsia than women who had low levels.

"This looks promising, but we need to do more research into how much and what type of chocolate is the most beneficial," Triche said.

—John Curtis

A VIPER'S VENOM AND STROKE

What does snake venom have to do with stroke? Depending on the results of a study in which Yale-New Haven Hospital (YNHH) is participating, possibly a lot.

Doctors at YNHH are administering ancrod, a drug derived from the venom of the Malayan pit viper, to eligible patients who enter the hospital with symptoms of acute ischemic stroke.

In such cases doctors may administer a clot-breaking agent—tissue plasminogen activator, or tPA—but it must be given no more than three hours after symptoms appear. Ancrod has an anticoagulant effect and can be administered up to six hours later. "If ancrod is safe and effective," said Joseph Schindler, M.D., assistant professor of neurology and neurosurgery and clinical director of the Stroke Center at YNHH, "it will double the time frame during which stroke patients can be treated."

YNHH is the only Connecticut hospital in the trial, which is expected to last one to two years.

-Charles Gershman

9

10



In this image of a developing embryonic rat spinal cord, the purple marks show growing commissural axons before they cross to opposing hemispheres. Yellow marks show a receptor called DSCAM, which is necessary to guide axons to their destinations.

Biologists find molecule that guides axons

A receptor implicated in Down syndrome and fruit fly development also charts a path for nerve fibers.

Like a complex electronic device, the "wiring" of the nervous system has no tolerance for error. As an embryo develops, wirelike axons sprout from cells, elongating to form networks of neurons in the brain and spinal cord. Some axons cross the body from one side to the other, while others stay put. Neuroscientists have long wondered how axons migrate to form trillions of connections among neurons. How do they know where to travel and when to cross? Molecular signals are at the heart of the puzzle.

The first such signal, a guidance molecule called netrin-1, was identified about 20 years ago. Since then, researchers have found receptors on the axons that help them steer toward their targets. Now Yale researchers have found another molecule that guides axons on their intricate journey.

A team led by Elke Stein, PH.D., assistant professor of molecular, cellular and developmental biology and of cell biology, reported in June in the journal *Cell* that it had discovered that a gene linked to mental retardation in Down syndrome is also essential for axons in the spinal cord to cross from one side of the body to the other.

The protein made from that gene is a receptor called DSCAM, which stands for Down Syndrome Cell Adhesion Molecule. DSCAM is already familiar to researchers. Its genetic instructions are on chromosome 21, and people with Down syndrome have three copies of the chromosome rather than the normal two.

The Yale scientists found DSCAM through studies of nerve fibers called commissural axons that cross at the midline of the spinal cord, which divides the body into its right and left halves. Cells at the midline instruct axons by secreting attractive and repulsive molecules. Netrin-1, the guidance molecule identified 20 years ago, is one such molecule. It attracts and guides commissural axons over long distances to the midline of the central nervous system. Researchers had previously found that netrin-I signals DCC, a receptor that steers commissural axons to their targets. But they noted that some axons migrate even when DCC is absent. There had to be another receptor involved, and scientists searched for it for more than 10 years.

The missing receptor, Stein's lab found, was DSCAM, which was known to regulate nervous system development in fruit flies. But in humans it had only been known to help neural cells adhere to each other, and was thought to contribute to mental retardation in people with Down syndrome. In collaboration with scientists from Genentech, Stein and graduate student Alice Ly found that DSCAM at the tips of migrating axons is required in order to cross the midline in response to the attractant, netrin-1, which activates DSCAM and initiates directional growth of commissural axons in much the same way that a key turns the ignition and starts a car.

The researchers showed that commissural axons that lack DSCAM lose their "sense of direction," fail to grow and don't reach the midline. The Stein laboratory is now investigating whether DSCAM plays a key role in wiring other parts of the nervous system and its contributions to mental retardation in Down syndrome.

—Jenny Blair

Bacteria disable immune cells by exploiting a genetic similarity

The bacteria that cause Legionnaires' disease and Q fever, both of which are linked to pneumonia, use a clever form of mimicry to survive inside host cells, according to a team of Yale scientists. Both bacteria use genes that have evolved in tandem with genes in their hosts and that disarm the immune system cells that are trying to kill them, the researchers reported in the journal *Science* in June.

"Because of their lifestyle, trying to identify how these organisms cause disease has been really difficult," said Craig R. Roy, PH.D., associate professor of microbial pathogenesis, referring to the fact that the bacteria live inside their host cells. Roy's team knew that some disease-causing bacteria inject proteins into human cells. What those proteins are and what they do, though, was unknown.

Previous research on the genomes of the bacteria, *Legionella* and *Coxiella*, had turned up many genes with areas called ANKS (ankyrin repeat homology domains). These genes bear a strong resemblance to important genes in eukaryotic cells, those cells with a nucleus that are found in humans and other advanced life forms. *Legionella* and *Coxiella* appear to have "hijacked" genes from their hosts in order to survive in the cell. In fact, some species of these bacteria cannot exist outside a eukaryotic cell.

Roy's lab showed that ANK proteins are secreted into macrophages immune system cells—and once inside, the proteins turn off mechanisms designed to destroy the bacteria. The macrophage ordinarily kills bacteria by exposing them to a destructive acidic environment, but the ANK proteins prevent the acidic compartment from being transported to the bacteria by mimicking a natural process that occurs during cell division.

Roy believes that more such survival tricks of gram-negative pathogens will be found, and that the diseases may one day be preventable with a vaccine that disables the ANK protein and allows macrophages to complete the job of destruction. "This study at least gives us a foothold," he said.

—J.B.



This image of a cell infected with *Legionella* shows host cell microtubules, which have been labeled using green fluorescent protein to show the bacterial compartments closely aligned on the microtubule network.

et cetera

11

METASTASIS AND A HYBRID CELL

Metastasis, the spread of cancer throughout the body, may be caused by a hybrid cell that takes on the most dangerous features of two different cell types, according to a review by Yale scientists in the May issue of *Nature Reviews Cancer*.

According to dermatology researchers John M. Pawelek, PH.D., and Ashok K. Chakraborty, PH.D., the natural hybrids take on both the white cell's migratory ability and the cancer cell's tendency to divide uncontrollably. The hybrid can travel to other organs and seed new cancer sites.

"This is a unifying explanation for metastasis," said Pawelek. "We expect this to open new areas for therapy based on the fusion process itself." So far, one case of fusion in humans and many cases in mice have been reported. Pawelek said more research is needed to be certain that fusion accounts for metastasis in humans.

A CLUE TO EVOLUTION

After 16 years of research, Yale scientists have produced the first images of a group II intron, a cellular molecule whose ancestor may have opened the door to the evolution of higher organisms.

Anna Marie Pyle, PH.D., professor of molecular biophysics and biochemistry, and her team crystallized the intron of a salttolerant bacterium that lives in the Sea of Japan. High-resolution images of the crystal, which appeared in *Science* in April, support the hypothesis that the intron shares a close evolutionary heritage with the human spliceosome, a complex molecular machine found in higher organisms that allows many proteins to be made from one stretch of the genome.

"The molecules showed us their structure, their active site and their activity," said Pyle. "We were even able to visualize their associated ions." Pyle hopes the introns may be developed into agents for gene therapy. —J.B.

When the doctor is the patient

Robert Klitzman's resistance to his own depression led him to explore what happens when doctors get sick.

Robert L. Klitzman, M.D. '85, expected the grief that followed the death of his sister Karen, who died at the age of 38 in the World Trade Center on September 11, 2001. But he did not expect that he would be unable to sleep and would suffer from persistent flu. Or that he would stop listening to music and take no pleasure in reading.

When friends told Klitzman that he was depressed, he rejected the idea. As a psychiatrist, of course, he knew that emotional depression often manifests itself in the body. "I'd read it in textbooks," he acknowledged. Eventually Klitzman did recognize that it was depression, not flu, that was making him feel that his body had "given way" beneath him. "Going through it myself made me realize how much I didn't know about what it was to be a patient," he said. That realization, he said, was "a defining moment."

Klitzman, a research scientist and associate professor of clinical psychiatry at the HIV Center for Clinical and Behavioral Studies at the New York State Psychiatric Institute and Columbia University, had already written five books. In fact, he'd gotten his start as a writer by reviewing books while a medical student at Yale—a starting point he recommends to students today. His role models included Richard A. Selzer, M.D., HS '61; Sherwin B. Nuland, M.D. '55, HS '61; and Howard M. Spiro, M.D.—Yale physicians who are also prominent authors. Klitzman had already contemplated writing a book about doctors as patients. Now, however, "It was no longer an academic question."

When Doctors Become Patients is the product of interviews with 70 physicians of all ages who were facing cancer, heart disease, Huntington disease, bipolar disorder, HIV and other illnesses. Klitzman analyzes such common themes as denial of illness, doctors choosing doctors, "self-doctoring," going public about one's disease, overworking, coping and the role of spiritual beliefs.

Klitzman found that the doctors viewed themselves either as patients or as doctors, "as if individuals had a zero-sum identity." In reality, Klitzman said, "They're not entirely doctors and they're not entirely patients." Klitzman called this "odd hybrid form" the "doctor-patient"—one doctor-patient with a foot infection brought his own bag of opiates to the hospital. And as patients, Klitzman's interviewees were often upset by the carelessness with which their doctors addressed their fears. A surgeon told one doctor-patient that a procedure carried a 5 percent chance of dying. The patient would rather have heard that he had a 95 percent chance of living.

Just as Klitzman resisted the notion of his own depression, his colleagues also denied that they were sick. They told him, "I feel like I have a magic white coat. Illness happens out there—not to me." Klitzman noted that magical thinking is part of our everyday lives: "When we blow out the birthday candles, we all make a wish." But doctors deny their irrationality, contending, "We do not engage in magical thinking. We're trained scientists."

Perhaps because doctors see themselves as scientists, they are reluctant to discuss religion or spirituality with their patients, as Klitzman's research suggests. Yet "when patients are lying in bed, that's what they're thinking about," he said. He advocates adding at least a lecture on the topic during medical school.

A reviewer wrote in the *New England Journal of Medicine* that Klitzman's book "goes to the very heart of the question of what a physician is." In addition, *When Doctors Become Patients* serves as a lasting memorial to Karen Klitzman.

-Cathy Shufro



Robert Klitzman's depression after the loss of his sister on 9/11 led him to explore what he calls the "odd hybrid" of doctors who become patients.

Bookshelf focuses on books and authors at the School of Medicine. Send suggestions to Cathy Shufro at cathy.shufro@yale.edu.

BOOK NOTES



Polarities of Experiences: Relatedness and Self-Definition in Personality Development, Psychopathology and the Therapeutic Process

by Sidney J. Blatt, PH.D., professor of psychiatry and psychology (American Psychological Association) The author proposes that psychological development is a lifelong personal negotiation between two dimensions: relatedness, which he terms the anaclitic dimension; and selfdefinition, or the introjective dimension. He contends that emphasis on one developmental line at the expense of the other. however, can lead to a variety of mental disorders. Within this framework. Blatt sees mental disorders as compensatory exaggerations of the normal polarities of relatedness and self-definition rather than clusters of present or absent symptoms. Blatt discusses research indicating that anaclitic and introjective persons respond differently to psychotherapy. He then argues that this conceptualization of personality development has clear implications for refining approaches to therapy.

The Kazdin Method for Parenting the Defiant Child: With No Pills,

No Therapy, No Contest of Wills by Alan E. Kazdin, PH.D., the John M. Musser Professor of Psychology, and director of the Yale Parenting Center and Child Conduct Clinic (Houghton Mifflin) In this book and DVD, Kazdin lays out his science-based program for using praise and rewards to alter children's behavior. Kazdin provides a step-by-step method that relies on positive reinforcement and a reward system for dealing with behavior problems. The book describes approaches for children of different ages; discusses ways to involve siblings; and provides scenarios for coping with such commonplace difficulties as tantrums, dawdling, resisting homework and delaying bedtime.

Saving Sickly Children: The Tuberculosis Preventorium in American Life, 1909-1970

by Cynthia A. Connolly, R.N., PH.D., assistant professor of nursing and the history of medicine (Rutgers University Press) The author provides an analysis of public health and family welfare viewed through the institution of the tuberculosis preventorium of the early 20th century. This facility was intended to prevent TB in indigent children at risk for developing the disease or who came from families labeled as irresponsible. Connolly further explains how the child-saving themes embedded in the preventorium movement continue to shape contemporary pediatric health care delivery and family policy in the United States.

Attachment and Sexuality

edited by Sidney J. Blatt, PH.D., professor of psychiatry and psychology; Diana Diamond, PH.D., and Joseph D. Lichtenberg, M.D. (The Analytic Press) Each paper featured in this text forms a separate narrative strand that clarifies different configurations of the relationship between attachment and sexuality. The unifying thread is the notion that the attachment system, and particularly the degree of felt security—or lack thereof—in relation to early attachment figures, provides a paradigm for relationships that forms a scaffold for the developmental unfolding of sexuality in all its manifestations. These manifestations include infantile and adult, masturbatory and mutual, and normative and perverse sexuality.

Apoptosis and Cancer: Methods and Protocols

edited by Gil Mor, м.D., PH.D., associate professor of obstetrics, gynecology and reproductive sciences, and Avesha B. Alvero, м.р., associate research scientist in obstetrics, gynecology and reproductive sciences (Humana Press) This book, a collaboration between academics and industrybased scientists, describes the performance of contemporary techniques for studying the biology of apoptosis and its role in cancer. The protocols described within will aid both academic laboratory workers interested in further characterizing the mechanism of apoptosis and industry-based researchers concerned with identifying new target molecules or screening for new compounds with potential clinical use. The text covers the newest methods as well as basic conventional techniques.

The Future of Medicine: Megatrends in Health Care That Will Improve Your Quality of Life by Stephen C. Schimpff, м.р. 'б7. нร 'бо (Thomas Nelson Publisher) This book describes and evaluates health care innovations in areas including genomics, imaging, pharmaceuticals, the operating room, and alternative and complementary medicine. The author combines scientific fact with personal stories and experiences to describe the tools, techniques and treatments that are making a difference in health care. These innovations include vaccines that prevent cancer and chronic disease; surgery simulation and robots in the operating room; and smaller, more powerful medical devices that help a patient's heart beat, relieve depression and replace failing organs.

Hip and Knee Surgery: A Patient's Guide to Hip Replacement, Hip Resurfacing, Knee Replacement and Knee Arthroscopy

by Robert E. Kennon, м.D., нs '04 (Lulu Publisher) This book contains information for patients considering treatment for hip or knee arthritis and related conditions. The author explains what to expect before, during and after hospitalization; describes postoperative exercises; and offers recommendations for rehabilitation. Illustrated sections discuss hip and knee surgeries; nonoperative treatment options; surgical approaches, the latest minimally invasive surgery techniques; implant materials and designs; and potential complications of joint surgery.

BOOKS & Ideas BOOK NOTES

IN CIRCULATION



Comfortably Numb

Neuroinformatics (Methods in Molecular Biology)

edited by Chiquito J. Crasto, PH.D., м.s., associate research scientist in neurobiology (Humana Press) This book describes advances in data sharing and the use of computational models in neuroscience. It provides expert summaries of specific computational models and simulations as well as approaches to data mining. The authors also discuss informatics representation and approaches to the structural complexity of the brain using a variety of both traditional and noninvasive imaging methods. The book's final section considers the value of using neuroinformatics to understand such complex mental disorders as dementia, schizophrenia and Alzheimer disease.

Comfortably Numb: How Psychiatry Is Medicating a Nation

by Charles M. Barber, M.F.A., lecturer in psychiatry (Pantheon) The author argues that without an industry to promote them, nonpharmaceutical approaches to reducing emotional distress are overlooked by a nation that sees drugs as instant cure-alls. He argues that Americans are under increasing pressure to selfmedicate. In analyzing these influences, Barber cites directto-consumer advertising; the promise of the quick fix; and the blurring of the distinction between mental illness-for which medication might be appropriate-and everyday emotional problems. Barber then offers therapeutic alternatives to prescription antidepressants.

Seldin and Giebisch's The Kidney: Physiology and Pathophysiology, 4th ed.

YOU TAKE THAT PILL

edited by Robert J. Alpern, м.р., dean of the School of Medicine and Ensign Professor of Medicine (nephrology), and the late Steven C. Hebert, M.D., former C.N.H. Long Professor of Cellular and Molecular Physiology and professor of medicine (nephrology) (Academic Press) This edition has more than 40 new chapters and 1,000 illustrations, providing comprehensive coverage of renal physiology and pathophysiology. The topics move from the molecular biology of the kidney and its cell physiology to clinical issues surrounding renal function and dysfunction.

Before You Take That Pill: Why the Drug Industry May Be Bad for Your Health

by J. Douglas Bremner, м.D., former associate professor of diagnostic radiology and psychiatry (Avery of PenguinGroup) The author offers an inside look at the pharmaceutical industry as well as a scientifically backed assessment of the risks of more than 300 prescribed medications, vitamins and supplements. This book distinguishes between the pharmaceuticals that are essential to the health of consumers and those whose benefits may not outweigh their potential side effects.

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

A Yale librarian upgrades Internet access for physicians in Uganda

When librarian Mark Gentry, M.A., M.L.S., set out to expand Internet access at a hospital in Uganda, he experienced déjà vu. "The speed of the Internet took me back 15 years to the beginning of the Web, when we had dial-up modems," said Gentry, the clinical support librarian at the Cushing/ Whitney Medical Library.

Gentry learned about the idiosyncrasies of satellitebased Internet service in Uganda when he joined the Yale-Makerere collaboration, a partnership that includes the School of Medicine, Makerere University and Mulago Hospital in Kampala. Since 2006 Yale attendings and residents have traveled to Kampala for rotations at Mulago Hospital, and Ugandan residents are now coming to Yale for clinical training.

While visiting Mulago Hospital in the spring of 2008, Gentry streamlined Internet use for physicians by setting up a home page that links directly to such often-used functions as e-mail and online journals. "*Click*: you go right to it. Because every time you get an intermediate page, you have to wait from 10 to 30 seconds," said Gentry. Meanwhile a Yale resident compiled CDs that allow Ugandan colleagues to bypass the Internet—the disks contain copyright-free information on diseases such as HIV, tuberculosis and malaria.

Gentry next began building up the library for the Department of Medicine at Mulago Hospital, where the medical textbooks were 20 years old. Gentry collected 50 essential texts that were hand-delivered to Kampala. Up-to-date books are a godsend, said Ugandan resident Fred Okuku, M.D. During a five-month rotation at Yale last spring, Okuku discovered journal articles about research done in Uganda that he'd been unable to access at home.

While in Uganda, Gentry promoted a free Internet service called HINARI; sponsored by the World Health Organization for health care workers in developing countries, it provides links to nearly 4,000 journals.

Gentry said the Makerere collaboration has been a natural extension of his work on Cedar Street. "Part of my job as a clinical support librarian is to do what I can to support our people wherever they are."

-Cathy Shufro

In Circulation focuses on activities at the Cushing/Whitney Medical Library. Send suggestions to Cathy Shufro at cathy.shufro@yale.edu.

ON CAMPUS



Autorith Lawsuits could bankrupt vaccine program

A program that encourages childhood vaccinations could collapse under unproven allegations that the shots cause disease, an expert warned at grand rounds for the Department of Pediatrics in May.

Paul Offit, M.D., chief of infectious diseases at Children's Hospital of Philadelphia, said that the fallout from a 2008 court decision would discourage vaccine makers from continuing production. Since 1955, when a bad batch of polio vaccine killed 10 people, testing and regulation of vaccines have improved. But subsequent court rulings that vaccine makers could be held liable without being negligent led to "a flood of lawsuits" in the 1970s.

In 1986 Congress created the National Vaccine Injury Compensation Program to protect vaccine makers while compensating those harmed by faulty vaccines. But Offit said that the program took "a sad turn" in 2008 when a special "vaccine court" composed of epidemiologists and clinicians ruled that claims can be granted even if it's only possible—with no epidemiological evidence—that vaccines are responsible.

About 5,000 children who claim to be harmed as a result of vaccination await a decision that could bankrupt the vaccine program. If the decision allows for monetary compensation, "it could eliminate the program," Offit said.

—John Dillon



A gene to protect bone marrow from chemotherapy

In a new approach to cancer treatment, researchers are studying a form of gene therapy that may make bone marrow more resistant to chemotherapy, allowing for higher doses and better outcomes.

"We are turning the tables," said Joseph R. Bertino, M.D., interim director and chief scientific officer of the Cancer Institute of New Jersey, at Yale Cancer Center grand rounds in May. "This therapy will allow for safer use of drugs and an increase in dosage. If we do this we can protect patients from a wide variety of chemotherapy drugs."

Bertino, who was director of the Yale Comprehensive Cancer Center from 1973 to 1975, said this approach calls for introducing a drug-resistant gene into hematopoietic progenitor cells. That could limit the drugs' toxicity and preserve the marrow's ability to produce infectionfighting white blood cells. Oncologists would then be able to prescribe higher doses of chemotherapy, potentially leading to improved outcomes.

Bertino said two clinical trials---one for lymphoma and another for pancreatic and breast cancer---are in the planning stages.

-John Curtis



Children, foster care and orphanages

When Nicolae Ceauşescu took power in Romania in 1965, he believed that his country needed a larger work force. He decreed, said Charles H. Zeanah Jr., M.D., Sellars-Polchow Professor of Psychiatry at Tulane University, that all women must bear five children.

The economy didn't improve, Zeanah told an audience at pediatric grand rounds in May, but more children entered the country's orphanages. "Children with a history of institutional rearing have a high risk of psychological and social problems," Zeanah said. In 2000, Zeanah and Charles Nelson, PH.D., of Harvard and Nathan Fox, PH.D., of the University of Maryland began a four-year study of 136 children who ranged in age from 7 to 33 months, and found that their development lagged in most areas. Half of the 136 children were then placed in foster care, previously unavailable in Bucharest, and half remained in institutions.

Foster care enhanced development in most areas, but complete recovery was rare. For cognitive development and attachment, recovery seemed to have more to do with the timing of interventions than their duration. Children who entered foster care before their second birthday, Zeanah said, were more likely to recover from the severe deprivations of Romanian orphanages.

—J.C.



Bolero, dementia and the creative process

In 1930, when Maurice Ravel composed *Boler*o, his best-known work, he may have been in the throes of frontotemporal dementia (FTD), a neurodegenerative disease that usually affects people in their late 50s. Ravel's meticulous handwriting had become irregular, he had lost his bags and tickets on a concert tour and, while conducting one of his works, he had uncharacteristically skipped from the opening movement to the coda.

In a talk at neuroscience grand rounds in May, Sarah C. Janicki, M.D., M.P.H., HS '08, said Ravel's case is not unusual—FTD has been linked to strong bouts of creativity. "Over time a series of patients were coming to light, patients with FTD developing creative skills," she said.

Although the reasons for this connection are not clear. the brain's left temporal lobe appears to be involved. And the disorder appears to release artistic inhibitions-artists move from representational to more abstract forms of expression. But as the disease progresses, that process reverses itself. "As [the patients'] language skills declined, their art became fairly representational instead of a creative manipulation to generate new thought," Janicki said.

—J.C.

A theory abandoned but still compelling



In 1977 readers were enthralled by *The Dragons of Eden*, a book by the astronomer Carl Sagan that explored the evolution of the human brain. *Dragons* won the 1978 Pulitzer Prize for general nonfiction and helped to launch Sagan's celebrity as a spokesman for science in the 1980s.

The real star of the book, however, was a theory of human neural organization that took root some 30 years earlier in writings by Paul D. MacLean, M.D. '40. MacLean, who died last December at age 94, was a highly original—some say eccentric—thinker whose model of the triune brain, though now discredited, has had a lasting cultural impact.

"Paul never traveled with the herd," said Thomas R. Insel, M.D., director of the National Institute of Mental Health, who worked alongside MacLean for 10 years at the Laboratory of Brain Evolution and Behavior in Poolesville, Md. Insel remembers his colleague as irreverent and uninhibited. MacLean once roamed through a room, Insel recalled, feeling the scalps of visiting scientists to ascertain the presence or absence of a skull protuberance he had deemed an important factor in the evolution of human intelligence.

The beginnings of MacLean's theory appeared in a 1949 paper just as he joined the faculty of the School of Medicine as an assistant professor of physiology with a joint appointment in psychiatry. After conducting electroencephalographic recordings in patients

OPPOSITE Paul MacLean believed that the neocortex was a relatively late development in the mammalian lineage, but there is now a consensus that homologues of this structure exist in simple fish, and even in insects.

BELOW In MacLean's triune brain (top), the neocortex has only partial dominion over the emotional responses of the more primitive limbic system (bottom). "This situation," he wrote, "provides a clue to understanding the difference between what we 'feel' and what we 'know.' "

In Paul MacLean's triune brain, primitive emotions overruled conscious thoughts.

with psychosomatic illnesses and epilepsy at Massachusetts General Hospital, MacLean had become convinced that the emotional components of these disorders were seated in deep brain structures that he called the visceral brain (and renamed the limbic system in 1952), which included the hippocampus, amygdala and cingulate gyrus.

Since all mammals possess variants of these structures. MacLean concluded that they are phylogenetically ancient and that the emotional responses they produce are only weakly regulated by such newer, human structures as the neocortex. "Our affective behavior continues to be dominated by a relatively crude and primitive system," he wrote. Twenty years later, MacLean rounded out his picture of the triune (three in one) brain by adding what he termed the R-complex (for "reptilian")-structures in the brain's core and brain stem that govern basic survival functionsto the neocortical and limbic systems he had defined previously.

The theory saw its fullest expression in MacLean's 1990 magnum opus, *The Triune Brain in Evolution*, which was based on wide-ranging anatomical studies of brains in animals as diverse as alligators and monkeys. In its casting of a cognitively sophisticated neocortex unable to fully restrain the primal emotional responses of the limbic system, MacLean's model was a neuroanatomical cousin to Freud's tripartite view of the mind, with its warring superego, ego and id. The theory's conceptual beauty and intuitive appeal lent it enormous staying power; it is still covered in many textbooks and course lectures in biological psychology.

But according to Terrence Deacon, PH.D., an expert on the evolution of human cognition at the University of California, Berkeley, subsequent research has revealed that MacLean's basic premise—his "'hats on top of hats' view" that brain systems were added by accretion over the course of evolution—was mistaken. "Adding on is almost certainly not the way the brain has evolved," said Deacon. "Instead, the same structures have become modified in different ways in different lineages."

Nonetheless, Deacon said, the force of MacLean's personality gave his ideas a special resonance. "His death represents the passing of an era, because he was really the model of the move towards understanding the brain in evolutionary terms," said Deacon. "A lot of our contemporary advances ride on top of his work, even though in hindsight it was misleading. That happens a lot in the sciences, and we don't often give credit to the false starts that really push us along the way."

Peter Farley is the managing editor of the bimonthly newsletter *Medicine@Yale*.

SPRIT





Mapping the future of medicine

Medical schools are relatively new to the game of large-scale clinical research; however, they are sponsoring studies to test new therapies with increasing frequency. With its largest grant ever, Yale is plunging headlong into human trials and assembling resources to help clinical scientists focus on ideas—and leave the red tape to others.

By Jill Max Illustrations by Jeffrey Fisher

About six years ago, Thomas O. Carpenter, M.D., professor of pediatrics (endocrinology), wondered why he was seeing an increasing number of infants with nutritional rickets. He examined some of the infants' medical records and found that although rickets is presumed to be caused by a vitamin D deficiency, fewer than half of the infants had low levels of the vitamin. Many appeared to be calcium-deficient as a result of being weaned from breast milk to juices and soda. With funding from the Gerber Foundation, Carpenter began a largescale three-year study in 2005 that involved 800 babies from inner-city New Haven health clinics and the Primary Care Center at Yale-New Haven Hospital. By screening infants at their well-child visits, Carpenter aims to define the prevalence of early rickets in New Haven, determine how much of it is due to vitamin D deficiency versus calcium deficiency and look for changes in biomarkers that can be spotted before bone disease is evident. The study is already showing results: Carpenter found that elevated levels of parathyroid hormone, which is used to diagnose rickets, can also be used to predict who may eventually develop the disease, so that doctors can begin to treat children to ward off the disorder before symptoms are present. He is also searching for other genetic factors that may represent an increased susceptibility to the disease.

Such clinical research is not a novelty at Yale. But these efforts are now being organized and supported on a much broader scale under the umbrella of the Yale Center for Clinical Investigation (YCCI). The center was launched in early 2006 to coordinate research programs among Yale's health science schools and the surrounding community. It is also intended to support faculty research efforts while at the same time ensuring that patients are protected and receive high-quality care. YCCI's mission dovetails with the National Institutes of Health (NIH) Roadmap for Medical Research, which was implemented in 2002 near the end of a five-year period in which Congress doubled the NIH budget. The Roadmap helped garner public support for NIH-supported research and provided a framework for bringing medical knowledge from the laboratory to the patient. In October 2006 the School of Medicine was one of 12 institutions around the country to receive a Clinical and Translational Science Award (CTSA); at \$57.3 million the five-year award is by far the largest NIH research grant in the school's history (see related story, page 24). When fully implemented in 2012, the CTSA initiative is expected to provide \$500 million annually to 60 academic health centers working in concert. NIH Director Elias A. Zerhouni, M.D., said that CTSA will "transform how clinical and translational research is conducted."

Yale has traditionally been strong in basic science and has been successful in identifying drug targets and such other methods of combating disease as tissue engineering or large-scale public health interventions aimed at disease prevention. But until recently a center for translating basic science discoveries into clinical practice had never taken hold.





"We just never had the necessary resources to set up the infrastructure we're able to have now," said Robert S. Sherwin, M.D., the C.N.H. Long Professor of Medicine and director of YCCI. The center is a one-stop shop that provides the support investigators need to translate their work from the bench to the bedside. YCCI is accomplishing this task through a mix of such initiatives as helping investigators implement their own clinical trials, nurturing a new generation of physician-scientists and clinical investigators, and supporting collaborations with local organizations to promote public health.

Expertise and an online database

No one is more cognizant of the difficulties of negotiating the clinical trial maze than Christopher K. Breuer, м.р., assistant professor of surgery (pediatrics) and pediatrics. Breuer and Toshiharu Shinoka, M.D., PH.D., director of pediatric cardiac surgery at Yale-New Haven Children's Hospital, have developed a technique for engineering blood vessels to connect the inferior vena cava to the pulmonary artery. Known as Fontan surgery, the technique corrects a single-ventricle anomaly-a heart defect in which a patient has a weakened or single ventricle instead of the usual two. Breuer starts by seeding mononuclear cells isolated from a patient's bone marrow onto a tube made from a synthetic material similar to that used to make absorbable sutures. The cells attach to the synthetic scaffold and form new tissue; as the tissue forms the scaffold degrades, leaving a purely biological vessel. Blood vessels grown from a patient's own cells are less prone to infection than the artificial vessels that have traditionally been used in this surgery. The natural vessels are biocompatible and-perhaps most important for pediatric applications-they grow with the child, precluding the need for further surgery.

When Breuer began experimenting with tissue engineering in the early 1990s, he broke down a blood vessel into its cellular components in order to grow a new one. But this approach required additional surgery to procure the blood vessel and up to four months to grow the cells in culture and allow them to attach to the scaffold. He can now perform a bone marrow aspiration, isolate a special fraction of stem cells, seed them onto the scaffold, and implant the engineered vessel into the patient in a single procedure that lasts about six hours.

Breuer is about to begin a Phase I study to test the procedure's safety. He plans to try it in six patients over the next three years, staggering enrollment so that each patient can benefit from the one before. Although Shinoka has successfully performed the procedure on 23 patients in Japan, the regulatory requirements in the United States are more demanding. "One of the biggest challenges is the regulatory requirements," said Breuer. "YCCI has offered a lot of help and expertise."

Breuer is now well versed in running a clinical trial. For other researchers who lack the experience to put together an effective study, however, YCCI offers expertise in trial design, regulatory issues, protocol development, biostatistics and epidemiology, budget and recruitment. The center also offers research nursing support, data management, laboratory services, and both inpatient and outpatient facilities to conduct trials. A new online database at yaletrials.org provides detailed information about all clinical trials at Yale, so that patients interested in a specific disease can search for a trial related to it. YCCI also integrates the efforts of Yale's institutional review boards (IRBS) into the process. These panels, comprising clinicians, faculty, students and members of the community, must approve every research project that involves humans. even a paper-and-pencil survey. The medical school's two IRBS meet weekly to discuss the several hundred new proposals and more than 1,500 requests to renew ongoing studies that come their way each year.

In the world of clinical trials, some studies, such as Breuer's work, attempt to treat an existing condition, while others try to answer basic questions about the course of diseases or ways to prevent them. Carpenter's work does both. His nutritional rickets study is helping doctors treat the disease before it can do damage, but he also conducts research on X-linked hypophosphatemia (XLH), the most common form of inherited rickets in the United States. XLH can lead to deformed bones and debilitating arthritis. Carpenter established the Yale Center for XLH, an NIH-sponsored Center of Research Translation (CORT), one of eight in the country that serve as a model of translational research in academic medical centers. Some of the center's projects interface with CTSA, such as clinical trials studying the effect of a medication specifically aiming to suppress the hyperparathyroidism that occurs with XLH. Carpenter is also conducting an observational study to characterize the disease in patients past childhood and he is trying to determine the chemical and skeletal features of XLH in older patients. "Understanding the disease has opened up a whole new mechanism of how minerals are regulated in the body," said Carpenter. That area of research includes new therapies applicable not only to XLH but also to other disorders in which the body's handling of phosphate has gone amiss, such as chronic renal failure.

Focus on training

Perhaps the single most important aspect of the CTSA—and by extension YCCI—is training young researchers to conduct clinical studies. "In the past, most physicians learned on the job, sort of like an apprenticeship," said YCCI Director Sherwin. "But the kind of sophistication that's now required to do clinical research and the kind of mentorship background you need to do research today are much more involved than a simple apprenticeship." The Investigative Medicine Program, which serves as the administrative home for the educational component of YCCI, was developed at the School of Medicine in 1999 to award the PH.D. to physicians training in clinical research. Under the CTSA it has expanded to offer courses to medical, nursing and public health students. In addition, 20 junior faculty members and senior fellows who are committed to careers in clinical or translational research have received 18-month grants for salary and research support through YCCI'S Scholar program. Drawn from the three Yale health schools, the grant recipients are pursuing research projects under the guidance of individualized mentorship committees. "We're investing in them like we invest in training a PH.D., which involves having people from diverse backgrounds looking at their work from different perspectives," said Sherwin.

The work of Mary E. Tinetti, M.D., director of the Yale Program on Aging, serves as an example of the kind of research the program strives to advance. While training in geriatrics more than 20 years ago, she recognized that a slew of health conditions—such as incontinence, delirium and injuries caused by falls—were neglected by the health care system yet have a major impact on quality of life and functioning.

Tinetti identified characteristics linked to an increased risk of falls and conducted a study to determine whether interventions targeting these risk factors would prevent falls and injuries. Until that time, most clinical trials focused on a single intervention; however, Tinetti and her colleagues developed a new multifactorial trial design in which patients receive a combination of interventions tailored to their particular risk factors. For example, the intervention for patients who experience a drop in blood pressure when moving from lying or sitting to standing consists of increased hydration, specific exercises to do before getting up, and a reduction in medications likely to affect blood pressure changes on standing. In the mid-1990s, Tinetti and colleagues followed a group of 320 patients and controls for two years and found that patients who received such interventions reduced their risk of falling by about 30 percent. The next step was to see whether this reduction in falls would also occur when real-world clinicians, rather than investigators, were responsible for carrying out the interventions. For the past eight years, she and colleagues have been conducting a study in the greater Hartford area to train health care practitioners to incorporate components of fall prevention into their practice. The real-world trial was funded by the West Hartford-based Donaghue Medical Research Foundation, said Tinetti, the Gladys Phillips Crofoot Professor of Medicine (geriatrics) and professor of epidemiology (chronic diseases) and investigative medicine.

In an article published in the *New England Journal of Medicine* in July, Tinetti and her colleagues reported that the fall prevention programs resulted in an 11 percent reduction in falls compared to the control group, and 10 percent fewer 22



fall-related hip fractures and head injuries. The reduced injury rate translated into some 1,800 fewer emergency room visits over a two-year period and health care savings estimated at \$21 million.

"The research is done," Tinetti said. "The next step is to put it into practice, by making physicians, nurses and physical therapists everywhere more conscious of fall risks among their patients and what can be done to prevent falls."

From bedside to community

Tinetti's application of her research to clinical practice ties in with another major goal of YCCI-forging research relationships with the local community to improve public health. The Community Alliance for Research & Engagement (CARE), supported in part by YCCI, fosters community-based research and translates these findings for the benefit of New Havenarea residents. "The specific goal of CARE is to go from bedside to the community," said Jeannette R. Ickovics, PH.D., deputy director of CARE and professor of epidemiology (chronic diseases) and public health and of psychology. The first major initiative of CARE was to sponsor a consensus conference in 2007 with more than 70 leaders from New Haven and Yale. CARE has awarded five grants totaling \$110,000 for pilot research projects—including childhood obesity and violence prevention. CARE also publishes a quarterly newsletter highlighting community-based health information about how research is conducted, and "CAREtips"—easily accessible recommendations based on faculty findings. "There are so many important discoveries at Yale that land in the major medical journals but never benefit our neighbors right here in New Haven," said Ickovics. "We're looking to take the work of excellent Yale scientists and really give the science away. Our goal is to improve health in New Haven."

Even when investigators reach the point where they are conducting trials with study participants, they often continue working in the lab. For example, as Breuer prepares for the clinical trial to implant tissue-engineered blood vessels in children, he is experimenting with mice to discover the mechanism that forms the new tissue. Working with colleagues in biomedical engineering, he has isolated the protein responsible for maintaining the vessel's lumen (inner cavity), a finding that may eliminate the need for bone marrow aspiration in the next generation of tissue-engineered grafts for humans. Every investigation has the potential to advance the prevention and treatment of disease. The structure provided by YCCI is helping clinical investigators from different disciplines to pool their efforts, learn from one another, and take advantage of their collective expertise. "That's how progress is," said Breuer. "Everyone adds their own tiny step, and in the end you've gone a long way." YM

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Patient-volunteers help find cures on medicine's front lines

Every day at the medical school, patients and control subjects undergo imaging tests, hop on treadmills and swallow medications in the name of advancing knowledge. Some do it to contribute to society and research, some are lured by the payments offered, and some hope to help find a cure and ease a loved one's suffering or that of future patients.

That last consideration is what motivated Kriste Gill to enroll her newborn twins in a study on early indications of autism. A speech pathologist with a professional interest in the study, Gill also has a 22-year-old brother with autism. "I get to give back to research for a disability that's very near to us," she said. For the past two years, Gill's babies have undergone developmental assessments. The exams are not physically invasive, and Gill has learned much about the twins' development. And if any signs of autism should surface, she's confident the research team would flag them and recommend next steps for further evaluation.

A different concern brought Jan Davey into the Kronos Early **Estrogen Prevention Study (KEEPS)**, a study to determine whether early menopausal hormone therapy prevents or delays heart disease. Davey, 61, has a 27-year-old daughter and sees the need for research that may benefit future generations of women. Participants commit to taking hormones or a placebo as well as undergoing periodic lipid profile tests and vaginal ultrasounds for four years. As a clinical research nurse in Cardiovascular Medicine and at Yale **Cancer Center, Davey understands** the demands and rewards of clinical trials but had never before participated in one. "It's a very

important part of what we do in health care," she said.

Some participate in hopes of obtaining treatment for a disease from which they or a loved one suffer. Terri Rathbun's 16-year-old daughter, Molly, has childhood absence epilepsy-short seizures in which the person appears to blank out. Her condition has not responded to medication. To assess Molly's brain function, she underwent MRI scans while performing cognitive tasks. Her mother is hoping the study will benefit other children: in the meantime, it has helped her recognize how well Molly has coped while living with seizures. According to her mother, Molly hopes that participating in this study "will open up opportunities for other kids so that seizures don't define their lives."

For cancer patients Kathy Willie and Geralyn Spollett, a trial for treatment of HER2-positive breast cancer was a chance to receive chemotherapy that might have reduced or eliminated their tumors before surgery. Willie initially didn't want to undergo chemotherapy, but her decision paid off; during a partial mastectomy her surgeon found no trace of the tumor. Although the treatment didn't change the course of Spollett's treatment-she ended up needing a mastectomy as well as chemotherapy and radiation-she believes it was a positive experience."I felt lucky to be in the trial because of the consultation and support," said Spollett, who will have follow-up blood work in September.

Social responsibility also motivates patients. Jean O'Brien, 65, and her daughter Stephanie, 32, have X-linked hypophosphatemia (XLH), the most common form of inherited rickets in the United States. They joined in a study designed to define the features of the disease in adults. "It's a few days out of my life that could change someone else's life," said Stephanie, referring to two days of bone scans, X-rays and ultrasounds at Yale-New Haven Hospital. "My generation is writing the textbook on this disease," said Jean, who hopes the study will benefit her grandson and future grandchildren.

Clinical trials require not only sick but also healthy subjects. One 76-year-old woman participates in the Alzheimer Disease **Neuro-imaging Initiative even** though she is healthy. As part of the three-year study she gets MRI and PET scans every six months so that researchers can compare the mental changes that occur in normal aging, mild cognitive impairment and Alzheimer disease. She hopes that the trial will lead to a cure that will help family members and friends who have the disease.

Because he has a family history of heart disease, 27-year-old Niall **McComiskey agreed to a stress** test on a treadmill, administration of adenosine to increase his heart rate and a PET scan. McComiskey also said that the \$200 he was paid didn't hurt, and for some people, financial compensation is reward enough. For others, it's a combination of factors that spur them to participate. One 40-year-old veteran, a recovering alcoholic and addict who suffers from post-traumatic stress disorder, had two reasons for undergoing PET scans as part of a study to measure the levels of neurotransmitters in brain tissue. He wanted to understand the chemical imbalances in his brain; he was also paid about \$700 to participate in the study. Thomas O. Carpenter, M.D., professor of pediatrics (endocrinology), offers a \$25 grocery card to participants in his nutritional study, which he said is an effective incentive.

Such are the rewards of clinical studies that patients often repeat the experience. Jan Davey, who is participating in the KEEPS study, has also signed up for three ancillary studies. "We wouldn't be where we are in health care if we hadn't been doing clinical research all these years," she said.

—Jill Max



Is the straight road too narrow?

Congressional demands for cures and accountability—combined with a flat NIH budget—have increased pressure on scientists to produce findings with direct application to disease. Nonetheless, there's great value in cultivating the art of finding what you're not looking for.

By Pat McCaffrey Illustrations by Jeffrey Fisher

The stereotype of the basic researcher—driven by curiosity, absorbed in the arcane, immune to practical considerations is only half right. The need to unravel a puzzle, to uncover the beauty and order in biological systems, or simply to follow one's nose, asking and answering questions, is both the initial impulse and sustaining force for many a career in basic research. Yet these scientists are not indifferent to the practical applications of their work. They are just not starting out with that particular end in mind.

Take structural biologist Thomas A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry. Beginning with his doctoral work more than 40 years ago, Steitz has fixated on one question: How do proteins and nucleic acids carry out their diverse jobs in cells? For Steitz, that question is best answered by looking at the macromolecule's shape; he is a leader in charting the topology of proteins and nucleic acids at the atomic level.

Steitz and his team were the first to see one particularly important biological machine eight years ago when they solved the molecular structure of the large subunit of the ribosome, the protein-making factory inside all cells. That discovery, coming after five years of effort, a few dead ends and a little luck, has turned out to have practical benefits. Many antibiotics work by interfering with the functions of bacterial ribosomes. Steitz's lab was soon busy looking at the ways in which antibiotics recognize and bind to the bacterial large ribosomal subunit and shut it down. Hard data about molecular interactions are like gold to scientists looking to design new antibiotics—as they are now doing in a company that Steitz helped found.

"When I started solving protein structures as a graduate student, I had no idea, nor did anyone else, that this would ever be of any practical benefit whatsoever," Steitz says. "We just wanted to know, how does this machine work? ... Our work has led to translational research, but it wasn't the goal. I never thought that I would end up building a pharmaceutical company around the study of the structure of the ribosome."

It is a cliché of scientific exploration that even the most esoteric work can yield unexpected benefits. From synthetic insulin, the first biotech drug (a result of studies of bacteria) to the latest frontier of RNA-based therapies (started by work in worms), Steitz posits that every single medical discovery of major importance made over the last 30 years has its roots in basic research. "If you trace back through the history of molecular biology, which made biotechnology possible, you find that it all came from basic research," he says.

So why are Steitz and his colleagues so worried about the future of creative, idea-driven biological research? He and researchers like him are proof that investments in ideas and individuals can and do pay off handsomely for human health. Nonetheless, these days a combination of painfully lean budgets at the government agencies that fund basic research, coupled with a current fashion for applied, diseaseoriented studies (see related story, page 18) have basic researchers asking where their next grant—not to mention the next generation of like-minded scientists—will come from.

Risk management

"What really gets me excited is a brand new project," says fruit fly researcher Lynn Cooley, PH.D., professor of genetics and cell biology.

Cooley is fascinated by egg production in female fruit flies, a process that reveals the ways in which the flies' cells communicate and cooperate in order to form nurturing environments for developing eggs. Although her work has some application to the growth and spread of human cancers, Cooley's research is guided by her team's latest experiments. "When a set of experiments opens doors to unexplored areas of biology, that's the fun part," she says. "That's what makes it exciting to go into the lab every day."

The harder part is finding the funding to support her quest. The bedrock of basic biomedical research in the United States has long been the investigator-initiated research grant from the National Institutes of Health (NIH), known as an ROI. These grants cover salaries and laboratory expenses for an investigator and a few junior scientists to work on projects of their own design. ROI grant applications are 25-page proposals that are reviewed by committees of researcher's peers, who judge their merits and recommend the best for funding. The system has worked well for years to cull out the most promising new research for NIH support.

And that research has been well supported. With a total NIH budget of \$29.5 billion in 2008, the United States leads the world in its funding of basic research in the biological sciences. Half of all federal funds devoted to scientific research are funneled to biomedical research through the NIH. That money pays for 80 percent of biomedical research done in the United States. Support for basic research boomed during the years between 1998 and 2003, when Congress oversaw the doubling of the NIH budget. The ROI program was a major beneficiary of the increase. "The fact is that the NIH has put us far ahead of the curve in biomedical research," says Cooley. "And we have seen a huge payoff from research at the extremely basic level. Look at the examples of therapeutic RNAS or stem cells. In both cases, the researchers were driven by curiosity as to how organisms develop from single cells to complicated systems. Who would have known that their work would become the underpinnings of some of the biggest therapeutic advances we'll see over the next decades?"

But what Congress gives, it can also take away. Since peaking in 2004, NIH funding has flatlined at \$29.5 billion, and next year's proposed budget looks to be more of the same. While Congress often kicks in a little more money to keep programs from further cuts, the effects of inflation mean that the NIH is operating with 13 percent less buying power than it had in 2004.

On top of that, the demand for ROI funding is higher than ever. During the doubling period, the whole research enterprise grew as universities and academic medical centers expanded basic research facilities and faculties. That expansion takes time, so the NIH saw only modest growth in the number of grant applications received during the doubling years. As a result, a larger proportion of grant applications were funded. In the first two years of flat budgets, however, the number of grant applications doubled as new researchers came on line, and success rates in obtaining grants plummeted.

There is no relief in sight. According to a budgetary analysis by the American Association for the Advancement of Science, under the proposed 2009 NIH budget, the number of new grants, the average size of a grant, and the expected success rate for grant applications are all expected to fall.

"I have two new projects I'm really excited about but also kind of nervous," admits Cooley. "The most exciting projects are the ones that are hardest to fund because they tend to be the risky ones—ones where our lab has no track record—and there's not a big field of established work to point to and show where we fit in."

Lean times force funding agencies like the NIH to be more conservative and favor surefire bets. That means that finding support for innovative science can go from difficult to impossible as budgets shrink, says Richard A. Flavell, PH.D., chair and Sterling Professor of Immunobiology, professor of biology and an HHMI investigator. "Grant reviewers still recognize research that is new and exciting and worth taking a chance on. But in a super-competitive environment, those off-the-wall, risky, creative projects lose out," he says.

Enter the Roadmap

Money, or lack of it, is not the only threat basic researchers perceive. Many report a growing unease with the wider world's view of their work, and with what some think is a mistaken assessment of its value. Among researchers, there is a palpable feeling that a recent and highly visible growth in support for clinically oriented translational research programs means less funding for basic research. In this regard, some re-searchers blame a set of programs collec(YCCI), under the direction of Robert S. Sherwin, M.D., the C.N.H. Long Professor of Medicine, received a \$57.3 million grant in 2006—the largest single NIH grant ever given to Yale. That grant included existing grants to Yale of \$25.8 million, so the net increase to Yale was \$31.5 million. Another recent NIH award supports the training of medical students to carry out clinical research.

No matter the merit of those programs, they create a perception problem, says Carolyn W. Slayman, PH.D., Sterling Professor of Genetics and deputy dean for academic and scientific affairs. Compared to an average RO1 grant of about \$1 million over four years, the new awards were eye-popping. "To starving scientists who are worrying about

"The NIH is not the Academic Scientist Employment Act. It's a mandate from Congress to create a biological basis for improved therapies and for improving health care". -Immunologist Jordan Pober

tively called the NIH Roadmap for Medical Research for draining support from their labs.

The Roadmap had its start at the end of the period of rapid budget growth. Anticipating that the public and its representatives in Congress would be looking for payoff on their investment, the then-new NIH director, Elias Zerhouni, M.D., initiated a mass consultation in 2002 with hundreds of scientists to identify gaps in NIH programs. Over the course of a year, Zerhouni identified areas in which the NIH might do a better job of supporting multidisciplinary teams as well as translational and clinical research. The process was dubbed the Roadmap; its first projects began in 2004.

There was controversy about the Roadmap from the beginning. Just as ROI funding was tightening, basic researchers watched money flow to translational research, multi-investigator grants and clinical research.

The School of Medicine has certainly benefited from that funding stream. The Yale Center for Clinical Investigation their own ROI, it's hard to see Roadmap grants awarded in huge and very visible chunks of \$20 or \$40 or \$50 million," Slayman says. "Their immediate reaction is, how many laboratories like mine could be kept going very happily for years with that money?"

Even so, the idea that the Roadmap is a drag on basic science funding is exaggerated, says Jordan S. Pober, M.D., PH.D., professor of immunobiology, pathology and dermatology and vice chair of the Section of Human and Translational Immunology.

The numbers support his view. Taken together, Road-map projects account for less than 2 percent of the total NIH budget; moreover, fully half of Roadmap funding goes to individual researchers in the form of ROI or similar grants. The real culprit, Pober says, is the stagnation of the overall budget. His message: "There is pain, to be sure. But don't blame the Roadmap, blame the budget." Moreover, the activities championed by the Roadmap are necessary for the NIH to fulfill its goal to improve people's health, Pober says. "The NIH is not the Academic Scientist Employment Act. It's a mandate from Congress to create a biological basis for improved therapies and for improving health care."

The Roadmap initiative just happened to come at the same time as the NIH budget stagnated and the chances to obtain ROI funding decreased dramatically, says Jeremy M. Berg, PH.D., the director of the NIH'S National Institute of General Medical Sciences, which primarily supports basic, nondisease-targeted research and is heavily involved in over the rocks in the field of biology and see what is underneath. And that means an investigator in a lab working steadily over years and decades. That means Steitz tinkering with the ribosome. It means Cooley finding out how flies make eggs.

That theme—the long and winding road from disease to cure—was echoed in a recent editorial in the journal *Science*. Editor in chief Bruce Alberts, PH.D., argued eloquently for the importance of basic research in spurring medical progress.

"We have all been taught that the shortest distance between two points is a straight line," Alberts writes. "But

We have all been taught that the shortest distance between two points is a straight line. But the same idea has repeatedly proven not to be true for progress in medical research? -*Science* editor Brace Alberts

Roadmap activities. "That does not mean those events are causally related."

On the contrary, Berg says, the Roadmap has been a very good thing for basic research. The idea of setting aside a relatively small amount of money for new kinds of programs and approaches was a key provision of the Roadmap and has paid off by becoming quite popular in Congress. "In my opinion the Roadmap has been quite successful with Congress in terms of their seeing the value in what we're doing. My sense is that the NIH would have been substantially worse off than we are right now if we had not had the Roadmap."

Shortest distance between two points

Money talk aside, researchers still worry that the hoopla surrounding new clinical and applied programs that began under the Roadmap may divert attention from the fact that successful medical research relies on a foundation of basic knowledge about the functioning of healthy cells and organisms. The only way to get that information is to turn the same idea has repeatedly proven not to be true for progress in medical research." The reason, he says, is that we understand so little of what there is to know about the basic functions of cells that researchers tracing a path from disease to cure must navigate largely uncharted terrain. Scientists continue to rely on lessons learned from simple organisms—yeast, bacteria, plants, fruit flies, worms—to guide progress through the terra incognita of human disease.

John Carlson, PH.D., the Eugene Higgins Professor of Molecular, Cellular and Developmental Biology, has been looking for answers in the fruit fly's sense of smell for 20 years. Carlson has spent that time figuring out the workings of odor receptors and the olfactory system of flies, which use their sense of smell primarily to navigate the world. He and his colleagues mapped out the chemical receptors and brain pathways involved in the uncanny ability of these pests to appear out of nowhere in response to the aroma of a banana left outside to ripen on a warm day. On the way, he has found both beauty and some unanticipated applications. "The same way that fruit flies find bananas, mosquitoes find humans," Carlson explains. "They both depend on their sense of smell." That insight propelled him into the field of malaria, a disease that infects hundreds of millions of people around the world each year. Carlson is working with European and African colleagues to find chemical compounds that confuse the sensory receptors on a mosquito's nose and prevent them from finding humans. In the future, he foresees using a similar approach to keep crops free of agricultural pests. Carlson says the work may also be adapted to use odor receptors as detection devices for explosives.

For two decades, Carlson has been able to keep his research program on track with an uninterrupted stream of funding from NIH. His applied research draws support from private foundations, including the Bill and Melinda Gates Foundation for the malaria work. Nonetheless, he says, "I do worry about the NIH dropping support for individual labs exploring questions that excite their curiosity about basic science."

The long view

The Nobel Prize-winning biologist Arthur Kornberg, M.D., liked to tell a story that starts with a surgeon out for his morning jog. While passing a lake, the doctor sees a man in the water about to drown. So he dives in, pulls the man out, resuscitates him and continues running.

A bit farther down the path, another man is flailing in the water in another part of the lake. The surgeon saves him, and no sooner sets off jogging again than he sees two more people in trouble in the water. He notices his friend, a neuroscience professor, loitering nearby and calls out for him to save one person while the surgeon rescues the other. When the neuroscientist does not move, the exasperated surgeon shouts at him, "Why aren't you doing something?"

The neuroscientist answers calmly, "I am doing something. I'm desperately trying to figure out who's throwing all these people in the lake."

The point is, of course, that the fight against human disease occurs on several fronts. Someone has to rush in and save today's victims. Solving fundamental problems, however, requires other people with different skills and interests. Neither group is more important than the other. That is one message that researchers fear is being lost on lawmakers and the public, and even on budding young scientists as the funding freeze continues.

Pietro De Camilli, M.D., Eugene Higgins Professor of Cell Biology and co-director of the program for Cellular Neuroscience, Neurodegeneration and Repair, sees this loss of perspective in his experience with up-and-coming researchers. "There is a perception I see in young people that if they want to be a scientist and successfully compete for funding, they have to work on applied problems. A career in basic research seems less and less attractive."

The boom-and-bust cycle of congressional appropriations to NIH over the last decade has left some senior researchers struggling to maintain long-term projects. When young investigators see their mentors not being funded, they get the message, says stem cell researcher Diane Krause, M.D., PH.D., professor of laboratory medicine and cell biology and associate director of the Yale Stem Cell Center. "This is dissuading people from trying to succeed as academic researchers. We certainly make it look difficult to our students and postdoctoral fellows."

At current levels, the NIH budget overall is a prescription for slowing medical progress in the future, not speeding it up, according to immunologist Flavell. He supports the Roadmap but cautions that any success depends on maintaining a healthy basic research environment and pushing forward with applied and clinical programs. One without the other makes no sense, yet increasingly he sees outstanding researchers unable to win grants. Unless something changes soon, he says, we may find ourselves 20 years down the road with an impressive clinical and translational infrastructure but few new basic findings to translate. YM

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Online: Yale Netcasts

Mapping the Ribosome. RICHARD FLAVELL: Mouse With a Human Immune System Could Revolutionize Research. PIETRO DE CAMILLI: Getting the Message.
A life's work in Indonesia

By Jill Max Photographs by Erick Danzer Kinari Webb came to medical school knowing how and where she wanted to practice medicine. Now, she and her ecologist husband are working to bring health care to a remote corner of Borneo while preserving the rain forest.



Kinari Webb, a 2002 graduate of the School of Medicine, visits with a family in the town of Sukadana in a remote corner of the Indonesian island of Borneo. Webb has opened a clinic that serves the local population. She and her husband are also working to preserve the rain forest of nearby Gunung Palung National Park. Webb spent a year traveling throughout Indonesia to find the right place to launch her clinic. Sukadana is next to a national park with a rain forest under siege from logging, and the region's three clinics and 60,000 people shared a single physician.



Pak Rudi, a 40-year-old from a remote corner of the island of Borneo, Indonesia, was in bad shape. Walking even a few steps left him short of breath. In the fall of 2007, with his wife and several family members, he traveled for eight hours by motorboat and motorcycle taxi to reach the coastal town of Sukadana, where he had relatives who urged him to seek help at the local clinic. By the time his

family carried him into the Alam Sehat Lestari clinic, known as ASRI, Pak Rudi was close to death. Although the clinic lacks an X-ray machine, the medical staff diagnosed Pak Rudi based on a physical exam and the medical history he and his family provided. Dilated cardiomyopathy due to a viral infection a decade earlier was causing his heart to fill almost his entire chest cavity—it was only later, after the doctors saw an old X-ray, that they realized how swollen the heart had been.

In Indonesia, which has 16 physicians per 100,000 people, 12 times lower than the ratio in the United States, medical care is a scarce commodity. In rural areas, the ratio is even worse: where Pak Rudi lived—in West Kalimantan three clinics and 60,000 residents shared one doctor. That changed when ASRI opened in June 2007 as the newest clinic in the area. A small house with three exam rooms and a lab for basic tests, the clinic is run by Kinari Webb, M.D. '02, who also led Pak Rudi's medical team.

"I figure there are not very many humans on the planet who are crazy enough to do something like this," says Webb, who spent a decade preparing to open her clinic in the rain forest. "Something like this" refers to her dual dreams of bringing health care to Borneo and promoting forest conservation. It's no accident that her clinic is next to Gunung Palung National Park—558 square miles of forest, swamps and mountains that contain 5,000 species of trees, wild orangutans, sun bears, agile gibbons, proboscis monkeys, wild boars and hundreds of bird species. This pristine habitat is in danger from logging companies and poachers who eke out a living by harvesting lumber. In the 1960s, rain forest covered 82 percent of Indonesia—now it covers 49 percent. Since the 1980s more than half the rain forest in Borneo, one of the largest of Indonesia's 17,500 islands, has been destroyed.

Webb first visited the island as an undergraduate at Reed College in Portland, Ore., and was both entranced by the beauty of Gunung Palung, with its mangrove forests and verdant mountains shrouded in gentle mists, and horrified by the extent of the region's illegal logging. While the government has tried to protect the rain forests through mass tree plantings and international carbon-trading schemes, villagers have few ways to earn a living. Some work on rubber and oil palm farms. Others earn a few dollars a week breaking boulders and selling the rocks to roadbuilding crews. More than 7 percent of the former Dutch colony's 245 million people live on less than a dollar a day. In ASRI's catchment area, many households survive on about \$15 a month, and for many families, a shared weekly egg is the sole source of protein. Tree poaching, although it pays less than \$2 a day, remains an attractive option.

A life-changing experience

In a sense, Webb's journey to Indonesia began during her childhood in Dixon, N.M., a small town about an hour from Santa Fe. Her parents, both of whom have PH.D.s in psychology, were hippies who had joined the back-to-theland movement and taught Webb and her sister a love of animals and nature. Webb majored in biology at Reed, where she focused on orangutans. She pursued her studies with a determination that would serve her well later: she went to the library, looked up articles on orangutans and asked every author for a job. In 1993, between her junior and senior years, she worked at a research station in Gunung Palung National Park, one of the world's few remaining orangutan habitats.

One day a research assistant approached her with a cut on the palm of his hand, and although the wound was not serious, he acted as if it were life-threatening. It dawned on Webb that for people living in remote areas a seemingly routine injury could have dire consequences. Since she had no medical training, Webb whipped out her copy of the health care manual *Where There Is No Doctor*, by David Werner, cleaned the cut and closed it with improvised butterfly

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BELOW Webb examines a woman in Sukadana. With limited resources and frequent power failures, Webb often improvises her treatment. She has used honey to treat a diabetic ulcer; cardboard to make inserts for shoes; and mucuna beans, with their high L-dopa concentration, to treat Parkinson disease. MIDDLE A family relaxes on their front porch in Sukadana. Webb has engaged the townspeople in a dialogue about conservation and offers health care credits at her clinic for those who promise not to engage in illegal logging.



bandages made of adhesive tape. The cut healed and Webb was hooked; she knew that she wanted to become a physician and that she wanted to help people in rural Indonesia.

Her experience at Gunung Palung was life-changing for other reasons as well. She met Campbell Webb, PH.D., a biologist and ecologist who was pursuing his doctorate at Harvard. At first they resisted romance in an isolated setting under the scrutiny of their colleagues. But candlelit dinners (there was no electricity), bathing in waterfalls (there was no plumbing) and two months alone at their camp weakened their resolve. They were married as soon as Kinari graduated from Reed.

In Gunung Palung the idea of the interconnectedness of living things took hold in Kinari Webb's mind. For several species of trees, for example, propagation depends on orangutans that eat their fruit and defecate the seeds. On a more global level, Webb realized that timbering not only reduced rainfall and lengthened the dry season, but also contributed to global warming. Webb decided to focus her energy on a new project: she would provide health care to a population in desperate need, but she would also use it as an incentive for villagers to stop cutting down trees.

A decade of preparation

More than 10 years passed before she could bring her vision to life. During that time she laid the groundwork for ASRI, whose name means "beautiful and harmoniously balanced." She came to Yale knowing exactly where she wanted to practice medicine. When it was time to apply for her residency, Webb looked for a family medicine program that would provide the best training for practicing medicine in a developing nation. At Contra Costa Regional Medical Center in Martinez, Calif., she delivered more than 250 babies and performed enough C-sections to qualify for privileges at any hospital in the United States. "She got this incredible preparation to be out in the middle of nowhere

RIGHT Webb and her husband, Cam, make their home in Sukadana, but the couple spend as many as five months of each year apart. Campbell Webb, a Harvard ecologist, travels throughout Indonesia and Malaysia for his work with the Arnold Arboretum.



and be the first person to do whatever has to be done," said Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93, associate dean for student affairs.

In early 2005, just before completing her residency, Webb returned to Indonesia to help in the aftermath of the tsunami that devastated coastal areas of more than a dozen countries on the Indian Ocean in December 2004. She was distressed to see that the efforts of many of the agencies and organizations were ineffective and little of the aid was reaching those who needed it most. This only fueled her determination to open her own clinic. After her residency, she set up Health in Harmony (healthinharmony.org), a nonprofit organization to manage fundraising. Cam Webb moved to Bogor, West Java, which his wife used as a base while she searched for a location that was both close to a rain forest and in an area with few health care resources. "The whole process was like stepping off a cliff," she said.

After almost a year of searching, Kinari Webb realized that Sukadana, just outside Gunung Palung, was the perfect spot. It's two airplane flights and a two-hour drive through mangrove swamps from Jakarta, Indonesia's capital. The heart of the park's forest is still uncut, so there is conservation work to be done, and the local population has unmet medical needs. The location also worked for Cam Webb, who got a job as a senior research scientist with Harvard and is working with the Center for Tropical Forest Science, the world's largest tropical forest research program. His work takes him from his home base in Sukadana to his office in Bogor, and to sites throughout Indonesia and Malaysia where he does research in plant biodiversity and teaches a Harvard field course on Bornean ecology.

Before she set up shop, Webb recruited college and medical school classmates to help raise start-up money through a combination of Indonesian and American grants and private donations. Despite support from the Indonesian government, Webb faced innumerable delays in securing permits to open her clinic. Every time she produced a document, bureaucrats demanded yet another. Even worse, officials had their hands out for bribes, which she refused to give.

On June 12, 2007, ASRI opened its doors. A fiveminute walk from an undeveloped beach, ASRI is on the outskirts of Sukadana (population 12,000), a sleepy town with a pungent fish market and several stores packed with flipflops, rattan baskets and plastic buckets. A forest stretches up the hills surrounding the village, and gibbons can be heard calling through the trees. Orange with a bright blue roof, the six-room clinic is surrounded by houses, rice fields and gardens. It has three exam rooms, a dental exam room and a room for patients to sleep overnight, plus a lab for malaria and TB smears, blood work and urinalysis. There is a small pharmacy with a refrigerator, but Webb would like to have a solar-powered model since the electricity blacks out as often as five times a day. When that happens Webb lights candles, and if an emergency requires electricity she turns on a generator. She would like to add an X-ray machine to the ultrasound, EKG machine and other equipment on hand.

The staff of 15 includes two Indonesian doctors, a dentist, three nurses, a pharmacy assistant, a conservation director and an organic farm manager. "Kinari has surrounded herself with a system that can support this project and she's sort of the spark in the middle, the lifeblood of the project," said Roger Barrow, M.D., associate clinical professor of family medicine at the University of California, Davis, who Gunung Palung National Park is one of the world's last habitats for orangutans, but logging, legal and illegal, has led to deforestation of more than 70 percent of Borneo's rain forest since 1980.



worked with Webb in the aftermath of the tsunami and visited ASRI in April 2007.

"What they were able to accomplish in four months is almost impossible to imagine in a country that moves that slowly," said Jeremy Sussman, M.D., who spent a few weeks at ASRI in November 2007 as part of the Johnson & Johnson Physician Scholars in International Health Program at Yale, which sends residents to underserved areas around the world. Webb appreciates the opportunity to tap into the expertise of volunteers like Sussman. "It's good for my doctors to have someone else teaching them besides me," she said. "It helps to have a wider variety of opinions and ways of doing medicine."

The clinic is already bursting at the seams—ASRI treated 3,000 patients in its first nine months and is booked three weeks in advance. Webb has started to think about a new building and plans to open a hospital. The nearest hospital is two hours away and anything more than minor surgery requires a seven-hour journey to Pontianak, the regional capital.

Because her resources are limited, Webb finds innovative ways to treat her patients, some of which she has picked up from visitors like Werner. Webb has used honey to treat a diabetic ulcer on a hand, fashioned cardboard shoe inserts for a boy who had trouble walking, and used mucuna beans from the clinic's organic garden (they have a high concentration of L-dopa, which increases dopamine levels) to treat Parkinson disease. She and her staff treated Pak Rudi with aspirin, diuretics and blood pressure medications. In June 2008, Webb learned that Pak Rudi had died; he went 34



With donations from the United States, Webb has been able to offer eyeglasses to villagers in Borneo. On a single day last year she handed out 93 pairs in one village.

off his medicines for a month, in part because of the difficulties of transportation from his village.

Patients with cancer, diabetes, high blood pressure, severe diarrhea and a variety of other ills come to ASRI, but the area's biggest health problem is tuberculosis. More than 20 percent of the local population has TB, Webb estimates, and she has trained and hired workers to institute a Directly Observed Therapy program, in which they visit patients to monitor them while they take their medications.

Poverty plays a major role in many of the diseases Webb treats and is also a barrier in receiving treatment, but Webb doesn't believe in free health care. "It's reasonable that you pay for it, but it's also reasonable that you pay for it in a way you can actually afford," she said. "It gives patients dignity." That's why health care credits are a key component of her program. Patients and their families can pay for their treatment by cleaning the clinic, doing laundry, washing equipment or providing manure for the organic garden. They can also undertake conservation work, as Pak Rudi's family did. During the month he spent recuperating at a nearby relative's house, his family worked in the organic garden next door to the clinic. Area villagers are learning organic farming, and vegetables from the garden feed the clinic staff and patients. Webb expects to have produce to sell in the local market to help pay for medicine and other supplies.

Linking health care to ecology

Getting the local population to understand why they should worry about the environment pervades almost everything Webb does. When asked why she and her colleagues bicycle instead of driving to the clinic, she says, "Because biking is healthier, cheaper and better for the environment." The clinic's staff held a series of meetings in villages surrounding Gunung Palung to discuss the connection between health and the environment and identify incentives that would motivate the villagers to protect the park from logging. It is here that Webb's effervescent yet soft-spoken demeanor works its charm. Indonesia is the largest Muslim nation in the world, but in West Kalimantan there are no restrictions on women's social liberties, and she engages villagers in lively discussions. ASRI's staff and local residents came up with a plan: communities would work toward a "green" conservation status, meaning no illegal logging in the previous month. In return, they receive one month of free ambulance service, mobile clinic visits and clinic discounts. No one is ever denied health care, but Webb would like to provide incentives for the long-term health of both the community and the environment. "We don't know yet whether the incentive is strong enough on an individual level or on a community level for people to actually change their behaviors," said Cam Webb, "but even if it doesn't work we're doing a lot of education. If we get even a portion of forest restored, then it's having a positive effect."

Although the program is still in its infancy, its reputation is spreading. The managers of an elephant conservation project on the Indonesian island of Sumatra have approached Webb about replicating the ASRI model. She hopes that other organizations around the world will also recognize its potential. Meanwhile, each day brings satisfaction that her vision is working. "I'm feeling kind of like a parent whose child has just started to toddle around," she said.

At the end of a long day treating patients, Webb will sometimes provide an evening meal to village children who stop by her thatched-roof house. Many of their neighbors consider the Webbs' house, with its cement floor and no plumbing, quite modest, but the couple finds it charming. A pump from their well fills a water tank on a hill that drains to a sink and they use a squat toilet which they flush with water from a bucket.

When Cam Webb is home, the two often paddle their dugout canoe to a small island, where they watch the sunset or go for a swim. When she's on her own, Kinari writes thank-you notes to donors and answers e-mail before falling into bed, where she may be awakened by a raucous serenade from gibbons camped out in the trees behind her house.

If she had any doubts about the course her life was taking, a recent boat ride into the park, where miles of grassland have replaced the once-majestic forests, convinced her that this is exactly where she wants to be and where her future lies. She plans on spending the next few decades in this remote corner of the world, but her patients hope the clinic will be around even longer, so that they won't have to worry whether a simple cut on the hand might end in tragedy. As one village leader put it, "We hope that ASRI will be forever and ever." YM

Jill Max is a freelance writer in Trumbull, Conn. Erick Danzer is a freelance photographer based in Indonesia.

Faculty



James Rothman

Leading cell biologist to head department

JAMES E. ROTHMAN, PH.D. '71, one of the world's leading cell biologists, has been named chair of the Department of Cell Biology and the Fergus F. Wallace Professor of Biomedical Sciences. Rothman will also launch the new Center for High-Throughput Cell Biology at Yale's West Campus, formerly the site of Bayer HealthCare.

Rothman came to Yale from Columbia University's College of Physicians and Surgeons, where he was a professor in the Department of Physiology and Biophysics, the Clyde and Helen Wu Professor of Chemical Biology and director of the Columbia Genome Center. Under Rothman's leadership Yale's Department of Cell Biology will be significantly expanded and will be co-located at the West Campus along with its present location at the main campus of the School of Medicine.

At the Yale Center for High-Throughput Cell Biology, Rothman will lead multidisciplinary teams of scientists to develop tools and techniques to rapidly decipher the cellular functions of the 25,000 known protein-coding genes in the human genome, providing fresh insights into disease and identifying new molecular targets for therapy. For more than two decades, Rothman has performed seminal research on membrane trafficking.

Rothman graduated summa cum laude from Yale College in 1971 with a degree in physics. His research interests were inspired by cell biologist and Nobel laureate George E. Palade, M.D., who founded Yale's Department of Cell Biology.

Rothman earned a PH.D. in biological chemistry from Harvard Medical School in 1976. He then spent two years as a postdoctoral associate in the laboratory of Harvey F. Lodish, PH.D., a preeminent biochemist at the Massachusetts Institute of Technology. In 1978, Rothman moved to the Department of Biochemistry at Stanford School of Medicine as an assistant professor. He continued his research at Princeton University from 1988 until 1991, when he became the founding chair of the Department of Cellular **Biochemistry and Biophysics at** Memorial Sloan-Kettering Cancer Center in New York and vice chair of the Sloan-Kettering Institute.

Rothman succeeds cell biologist and immunologist Ira S. Mellman, PH.D., who was chair and Sterling Professor of Cell Biology at the School of Medicine until 2007, when he joined the biotechnology company Genentech as vice president for oncology research. James D. Jamieson, M.D., professor of cell biology and director of the medical school's M.D./PH.D. program, served as interim chair of the department.



Joan Steitz

Yale professor receives Albany prize

JOAN A. STEITZ, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry, is one of the first two women scientists to receive the Albany Medical Center **Prize in Medicine and Biomedical** Research, America's top award in medicine. She shared the award with Elizabeth H. Blackburn, PH.D., FW '77, SC.D.H. '91, the Morris Herzstein Professor of Biology and Physiology at the University of California, San Francisco, The two will share the \$500,000 award. Now in its eighth year, the prize is the largest in medicine in the United States and the second largest in the world outside of the Nobel Prize

Steitz is best known for her pioneering work in RNA. She discovered and defined the function of small ribonucleoproteins (snRNPs) in pre-messenger RNAthe earliest product of DNA transcription-and was the first to learn that these cellular complexes (snRNPs) play a key role in processing messenger RNA by excising noncoding regions and splicing together the resulting segments. Her breakthroughs into the previously mysterious splicing process have clarified the science behind the formation of proteins and other biological processes, including the intricate changes that occur as the immune system and brain develop.

Steitz earned her PH.D. from Harvard in 1967. After completing postdoctoral work in Cambridge, England, she joined the Department of Molecular Biophysics and Biochemistry at Yale as an assistant professor and later became an associate and full professor, as well as chair of the department.



Pasko Rakic

Kavli Prize for a Yale neuroscientist

PASKO RAKIC, M.D., PH.D., chair and the Doris McConnell Duberg Professor of Neurobiology, professor of neurology and director of the Kavli Institute of Neuroscience at Yale, was named one of the inaugural recipients of the Kavli Prize, given for the first time this year. The 2008 laureates were selected for groundbreaking research that has significantly advanced understanding of the unusual properties of matter on an ultra-small scale, the basic circuitry of the human brain and the nature of quasars. Rakic, one of seven scientists to receive the \$1 million prize, was honored for a pioneering series of anatomical studies carried out over the past three decades that revealed how neurons in the developing cerebral cortex are generated and how they assemble themselves into interconnected circuits that direct higher-order sensory and motor functions. The seven winners will receive a scroll, a medal and a share of the overall prize for each area.

Faculty NOTES



Jack Elias

Andrew

Hamilton





Harlan Krumholz

Michael Snyder



Mary Tinetti

19



Amy Arnsten

Henry Cabin

Seven faculty members of the School of Medicine were elected to the Connecticut Academy of Science and Engineering. They are Jack A. Elias, M.D., Waldemar von Zedtwitz Professor of Medicine and chair of the Department of Internal Medicine; Andrew D. Hamilton, PH.D., provost of the university and the Benjamin Silliman Professor of Chemistry; Diane S. Krause, M.D., PH.D., professor of laboratory medicine and cell biology; Harlan M. Krumholz, M.D., the Harold H. Hines Jr. Professor of Medicine and professor of epidemiology and public health and investigative medicine; Nancy H. Ruddle, PH.D., the John Rodman Paul Professor of Epidemiology and Public Health and professor of immunobiology; Michael P. Snyder, PH.D., the Lewis B. Cullman Professor of Molecular, Cellular and Developmental Biology and professor of molecular biophysics and biochemistry; and Mary E. Tinetti, M.D., the Gladys Phillips Crofoot Professor of Medicine and professor of epidemiology (chronic diseases) and investigative medicine.

Amy F.T. Arnsten, PH.D., professor of neurobiology, was selected by NARSAD in April to receive its prestigious Distinguished Investigator Award. NARSAD will provide a one-year grant of \$100,000 to advance her research on schizophrenia. Arnsten's past work on prefrontal cortex and executive function has contributed to the development of new treatments for attention deficit disorder. In April two faculty members were awarded 2008 Young Investigator Awards from NARSAD, the world's leading charity dedicated to funding research on psychiatric disorders. They are among 220 earlycareer scientists in the United States and 11 other countries who will receive funds this year from NARSAD to advance their research on mental illnesses. Each will receive \$60,000 over the next two years. Savita G. Bhakta, M.B.B.S., plans to gain a better understanding of how cannabinoids (chemical compounds found in marijuana) induce schizophrenia-like behavioral and cognitive effects in healthy people and exacerbate symptoms in patients with schizophrenia, Fei Wang, PH.D., will use multimodal MRI technology to study adolescents with bipolar disorder. The study will identify abnormalities in the structural integrity of connections in brain circuitry serving the emotional processing that are implicated in the illness, as well as associated disruptions in circuitry function.

Henry S. Cabin, M.D., professor of medicine (cardiology), has been named medical director of the Yale-New Haven Hospital (YNHH) Heart and Vascular Center. Cabin will be responsible for day-to-day operations associated with the cardiovascular service line, including inpatient services, and diagnostic and interventional catheterization laboratories. In addition, Cabin will participate on an executive council and work collaboratively with other multidisciplinary physician leaders in medicine, radiology and surgery to build a comprehensive cardiac and vascular center. Since 1994,

Cabin has been associate section chief of cardiology at YNHH and associate chair, Department of Internal Medicine.

David C. Cone, M.D., associate professor of surgery (emergency medicine) and of epidemiology, has been appointed editor in chief of *Academic Emergency Medicine*, the journal of the Society of Academic Emergency Medicine.

Stephen C. Edberg, PH.D., professor of laboratory medicine and director of the Yale-New Haven Hospital microbiology laboratory, has been awarded the American Society for Microbiology's BD Award for Research in Clinical Microbiology. This award honors a clinical microbiologist for outstanding research accomplishments leading to or forming the foundation of important applications in clinical microbiology. Edberg's contributions to clinical microbiology range from basic science, through applications and technology transfer, to critical analysis of current microbiologic findings and principles as applied within the context of public health problems. His research has resulted in more than 180 publications.

Richard L. Edelson, M.D., director of Yale Cancer Center, has been named the inaugural Aaron B. and Marguerite Lerner Professor of Dermatology. Edelson has made fundamental contributions to the study of cutaneous T-cell lymphoma (CTCL), a disease caused by malignant T lymphocytes that affects the skin. He identified and characterized this cancer and his research group played a central role in deciphering the basic biologic properties of CTCL cells, both in delineating the pathogenesis of the malignancy and in developing effective therapies for it. Along with his research team, Edelson devised and implemented the first FDAapproved selective immunotherapy for any cancer, a treatment now referred to as transimmunization. This treatment has been administered worldwide to patients with CTCL and has proven to be a safe and clinically effective cellular "vaccine" for CTCL patients. Since 2003 Edelson has been director of Yale Cancer Center. In January he announced he would step down once a successor is appointed.

Christine Jacobs-Wagner, PH.D., the Maxine Singer Associate Professor of Molecular, Cellular and Developmental Biology, has been designated a Howard Hughes Medical Institute investigator. She is one of 17 Yale scientists who now hold the prestigious appointment. Jacobs-Wagner is one of the world's leading experts on the internal cellular workings of bacteria. Her descriptions of the inner mechanisms of bacteria have led to an appreciation of the survival strategies of these ancient organisms and new insights into how to study modern human illnesses.





Richard Edelson

David Cone



Christine

Jacobs-Wagner



Brian Smith



Ronald Vender

Ruslan Medzhitov, PH.D., received the Howard Taylor Ricketts Award from the University of Chicago in May. The Howard Taylor Ricketts Award is given in memory of Ricketts, the scientist for whom the *Rickettsia* genus of microorganisms is named. The award recognizes an individual who has made an outstanding contribution in a field of the medical sciences.

Curtis L. Patton, PH.D., professor emeritus in the School of Public Health, was one of 13 people to receive a Seton Elm/Ivy Award this spring. Patton was honored for bringing previously unrecognized African-Americans to public light. Yale's recognition of Edward A. Bouchet, a distinguished New Havener, Yale College's first African-American graduate and the first African-American to earn a PH.D. anywhere in the nation, is due in part to Patton. He also celebrated the work and legacy of Cortlandt Van Rensselaer Creed. M.D., another distinguished New Havener and the first African-American graduate of Yale University. In 2007, on the occasion of the 150th anniversary of Creed's graduation from the School of Medicine, Patton and his colleagues organized a series of events culminating in the dedication of a new memorial to Creed at the Grove Street Cemetery.

Joel L. Rosenbaum, PH.D., professor of cellular and molecular biology, received an honorary degree from the University of Siena in Italy, in May. Rosenbaum has been studying the ultra-structure of the intraflagellar transport (IFT) process at the University of Siena with his colleagues there. IFT was discovered in the Rosenbaum laboratory in 1992 and was shown to be responsible for the formation and maintenance of almost all cilia and flagella. Analysis of the genes underlying the IFT process have led to new insights into the role of cilia and flagella in polycystic kidney disease and other human diseases.

Brian R. Smith, M.D., professor and chair of laboratory medicine, has been elected president of the Academy of Clinical Laboratory Physicians and Scientists, the major academic society for laboratory medicine.

Edward L. Snyder, M.D., professor and associate chair for clinical affairs in the Department of Laboratory Medicine, has been voted president-elect of the National Marrow Donor Program. He will begin his twoyear term in January.

Scott A. Strobel, PH.D., professor of molecular biophysics and biochemistry, has been awarded the Schering-Plough Research Institute Award. The award is given by the American Society of Biochemistry and Molecular Biology to recognize outstanding scientific contributions made by young researchers early in their careers. Strobel gave the award lecture, "Three Views of RNA Catalysis: Ribozymes, Ribosomes and Riboswitches," at the society's annual meeting in San Diego in April.

Ronald J. Vender, M.D., '77, HS '80, FW '82, a nationally recognized gastroenterologist who specializes in therapeutic endoscopy and inflammatory bowel disease, started on June 1 as chief medical officer (смо) for Yale Medical Group (YMG) and associate dean for clinical affairs at the School of Medicine. He reports to David J. Leffell, M.D., chief executive officer of YMG and deputy dean for clinical affairs. Vender, a clinical professor of medicine, built a clinical practice in the New Haven area and has held leadership and teaching roles at Yale-New Haven Hospital, the Hospital of Saint Raphael and Milford Hospital. He chaired the National Affairs Committee of the American College of Gastroenterology and currently serves on the board of trustees. He has published numerous research papers with colleagues on the Yale faculty. One of the appeals of his new position is the chance to return to his alma mater and work with colleagues he's known since he was a student. "There are a number of people with whom I was a resident who are on the faculty. Some of my teachers and mentors are still here," Vender says. "I am being very warmly and generously received by my colleagues and former mentors. I feel that I am coming back to a place I never left."

SEND FACULTY NEWS TO

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The Class of '08



Liza Goldman Huertas, James Troy, Amy Meadows and Alexander Diaz de Villalvilla before the Commencement ceremony at Old Campus.



ABOVE Class co-president Kristina Zdanys received her degree from Dean Robert Alpern.

RIGHT Zofia Piotrowska, Karl Laskowski, Lu Anne Dinglasan and Kevin Lau on their way to Old Campus.



Celebration, loss and an exhortation to dream

Marking their own graduation, students in the Class of 2008 remembered a fallen classmate.

Commencement was a day of mixed emotions for graduates in the Class of 2008. As they celebrated their own passage from students to physicians, they also mourned the loss of their classmate Mila Rainof, who died on April 20 after being struck by a car. (See related story, page 4).

Rainof's absence was palpable throughout the day's events. As the medical and public health students marched to Old Campus, each left a carnation at the site of the accident at York Street and South Frontage Road. During the ceremony on Harkness Lawn, Merle Waxman, M.A., associate dean, ombudsperson and director of the Office of Women in Medicine, accepted Rainof's posthumous medical degree. And the class gift was a donation to a scholarship fund in Rainof's memory.

Maggie Samuels-Kalow and Ellen House took the podium to offer their reflections. They recalled Rainof's commitment to her friends and patients as well as her seemingly boundless warmth and compassion. Samuels-Kalow urged her classmates to find other ways to remember Rainof. "We honor her memory in less tangible ways, in the ways we treat each other and our patients," she said.

"Let's celebrate today, as Mila would have wanted us to," said House.

Commencement speaker Alfredo Quiñones-Hinojosa, M.D., offered as inspiration his own life story, recounting how he packed his few possessions into a bag 20 years ago and, with \$65 to his name, crossed the border illegally from Mexico to California. The same hands that now probe "the most beautiful organ in the human body the brain" were once bloody and raw from pulling weeds on the farms of the San Joaquin Valley. After an industrial accident almost killed him, Quiñones-Hinojosa's father told him, "You have been given a gift. Life is short."

Quiñones-Hinojosa went on to graduate from a California community college and Harvard Medical School. While at Harvard he became a U.S. citizen. He is now a neurosurgeon at the Johns Hopkins School of Medicine. (For the full text of the address, visit medicine.yale.edu/ysminfo/top_story/ 2008/05/commencement_speech.html)

Commencement awards

This year's Bohmfalk Prizes for excellence in teaching went to Leigh V. Evans, M.D., HS '02, assistant professor of surgery (emergency medicine), for clinical sciences, and to Aldo J. Peixoto, M.D., associate professor of medicine (nephrology), for basic science.

Thomas P. Duffy, M.D., professor of medicine (hematology), received the Leonard Tow Humanism in Medicine Award. The Leah M. Lowenstein Awards went to Nina Horowitz, M.D., assistant clinical professor of surgery, and to Andres S. Martin, M.D., M.P.H. '02, associate professor in the Child Study Center and of psychiatry.

Eve R. Colson, M.D. '89, associate professor of pediatrics, received the Alvan R. Feinstein Award. Lynn D. Wilson, M.D., M.P.H. '86, professor of therapeutic radiology and of dermatology, received the Francis Gilman Blake Award. And the Betsy Winters House Staff Award went to Vikram Reddy, M.D.

—John Curtis





ABOVE Deans Nancy Angoff and Richard Belitsky before the procession to Old Campus.

LEFT Former Beatle Sir Paul McCartney was among those who received an honorary doctorate from Yale this year.

students commencement 2008

Public health grads urged to develop skills beyond science as leaders and advocates

The 108 graduates of the School of Public Health's Class of 2008 have their work cut out for them: defeating the AIDS virus, reducing obesity and eliminating health care disparities to name just a few of the tasks cited by Dean Paul D. Cleary, PH.D. And they'll face one more challenge, said Commencement speaker Georges C. Benjamin, M.D., director of the American Public Health Association: "Nobody's going to know what you do," he told the graduates gathered in Battell Chapel on May 26.

Benjamin offered an analogy: Two people rescue a drowning person who drifts by their picnic spot. The next day they save two more people; and as the numbers steadily increase, they establish an elaborate rescue system using boats, ambulances and helicopters. When the rescuers finally address the cause of the problem—a curve in an upstream road—and solve it with a guardrail and speed limit, the flow of victims ends.

To achieve this sort of prevention, Benjamin told the graduates they'd need skills as leaders, administrators and advocates and good relationships with policy-makers. "Science is necessary but not sufficient," Cleary said, noting that students on the medical campus are pressing New Haven officials to improve traffic safety at nearby intersections. In April a medical student was killed (see related story, page 39); in October 2006 a public health student was seriously injured. Both were struck by cars.

Public health awards

This year's excellence in teaching award went to Annette M. Molinaro, PH.D., assistant professor of public health (biostatistics). "If you can generate enthusiasm for core biostatistics, you are *some teacher*," Cleary quipped.



Sharing the Dean's Prize for Outstanding M.P.H. Thesis were Rupak Datta, Ling-I Hsu, Diane Martinez and Stephanie Smith. The Henry J. (Sam) Chauncey Jr. Inspiration Award went to Heather McPheron, and Ashley Fields won the Cortlandt Van Rensselaer Creed Award. Student speaker Rebecca Boulos offered warm memories of

-Cathy Shufro

her classmates.



ABOVE Graduate Daina Barauskas with faculty member Annette Molinaro.

RIGHT Public health students proceed to Old Campus.



PA students don white coats in new ceremony marking their entry to medicine

Second-year students in the Physician Associate (PA) program helped their 37 first-year colleagues in the Class of 2000 don the white coats that symbolize the medical profession on the afternoon of March 20. Medical students have long participated in this tradition, but it is only the second time that Yale PA students have joined in the ritual. And unlike their medical colleagues, they celebrated not the beginning of their training, but a different milestone. The donning of the white coat in the Medical Historical Library marked the transition from learning in the classroom to learning on the wards from real patients.

"We wanted to incorporate into a ceremony the idea of trying to instill in the students the ethical responsibility of being health care providers and the reverence with which they should practice," said Mary L. Warner, M.M.Sc., PA-C, director of the PA program.

"The White Coat Ceremony is a rite of passage, serving as a reminder of your need to balance excellence in the medical sciences with demonstrated compassionate care," said keynote speaker Cynthia B. Lord, PA '91, director of the Quinnipiac University PA program and president-elect of the American Academy of Physician Assistants. "The white coat should never be a symbol of status, hierarchy or power."

—Melinda Tuhus





ABOVE At the White Coat Ceremony for students in the Physician Associate Program, second-year students helped first-years don the coats that symbolize their entry into clinical medicine. In turn, the first-year students placed School of Medicine pins on the coats of the second-years. Thea Cogan-Drew, president of the first-year class, right, put a pin on Karen Edwards' coat.



TOP Michelle Smith smiled as she got help from Tamara Brining.

ABOVE Jason Fleury helped Megan Dieterich don her white coat. 42

Students present their findings at 22nd Student Research Day

At this year's Student Research Day, the 22nd Annual Scientific Poster Session featuring research by students in medicine and public health, 58 students presented their findings on topics ranging from the soon-to-be-personal (*Depression and Resilience During the First Six Months of Internship*) to the practical (*Educational and Behavioral Interventions to Reduce Exposure to Isocyanates in Auto Body Shops*) to the profound (*Beyond Patient Satisfaction: Physician Ambivalence, Authenticity*





TOP Jennifer Dominguez, center, with colleagues from the Yale Program for Women's Reproductive Behavioral Health, where Dominguez did her thesis research.

A BOVE Amanika Kumar, a student from Stony Brook University Health Sciences Center School of Medicine, who was at Yale on a fellowship, with David G. Nathan, who delivered the Farr Lecture. and The Challenges to Patient-Centered Medicine).

Some projects reflected the notion that the most common expression in science is not "Eureka!," but "Huh?" As medical student Kiera S. Levine analyzed her findings—patients expressed satisfaction with physicians whose manner was cold and impersonal—she asked, "That's interesting. What's going on?" Her conclusion: "The idea of satisfaction is complicated and tremendously ambivalent. Looking for simple assessments doesn't reflect the patient's circumstances."

Medical student Aval Aizer-Radical Prostatectomy Versus Intensity-Modulated Radiation Therapy in the Management of Localized Prostate Adenocarcinoma—reviewed the records of about 800 patients treated for prostate cancer at Yale over a 10-year period to see whether they fared better with surgery or radiation therapy. For patients with a favorable prognosis, there was no difference in outcomes between patients who had surgery and those who had radiation. Patients with a poor prognosis tended to do better with the radiation therapy, as did patients with the most advanced cancers.

Allison Arwady, who graduated with a degree in medicine this year, studied an old disease that is on the rise again in New Haven and elsewhere. In her project, *The Uses of Rickets: Race, Technology and the Politics of Preventive Medicine in The Early 20th Century,* she found that in the century's early decades, as higher rates of the disease were observed in people with darker skin, it was erroneously concluded that the disease must be the result of poor sanitation. A large-scale study in New Haven in the 1920s found that the disease, now known to be caused by a vitamin D deficiency, was widespread and afflicted people of all races and ethnic groups. Only then, Arwady said, did the public stop blaming the victims.

She believes there's a lesson to be learned from this rush to judge and stereotype, as she sees that reaction reflected in the response to some public health issues we face today, such as HIV/AIDS.

Following the poster session, five students who won prizes for their research gave oral presentations. Lu Anne Dinglasan discussed "The role of matrix metalloproteinases in axon guidance and neurite outgrowth"; Ryan Kaple wrote his thesis on "The axial distribution of lesion-site atherosclerotic plaque components: An in vivo volumetric intravascular ultrasound radiofrequency analysis"; Jason Roh's talk was "The chemokine мср-і is an essential mediator in tissue engineered blood vessel development"; Andrew Simpson researched "The utility of plain radiography in the evaluation of degenerative spine disease"; and Nandakumar Narayanan's paper was titled "While they wait: Rodent frontal cortex and delayed-response performance."

The day ended with the annual Farr Lecture, delivered this year by David G. Nathan, M.D., president emeritus of the Dana-Farber Cancer Institute. His talk, "A voyage in clinical research," focused on his pioneering investigations into blood disorders.

—Jennifer Kaylin

Sarah Frasure, right, got a congratulatory hug from classmate Lindsay McGuire at Match Day in March.

Match Day 2008

Nationally, this year's match was the largest ever—more than 28,000 applicants competed for 22,240 slots as firstyear residents. At Yale, 97 students matched. And for the third time in the last four years, all students found a match. "I couldn't be happier," said Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93, associate dean for student affairs. This year's match also saw a high number of students entering psychiatry—nine chose the field, the most ever at Yale.

California

Alameda County Medical Center, Oakland

Mary Hatcher, emergency medicine Mila Rainof, emergency medicine

California Pacific Medical Center, San Francisco

Sean McBride, medicine-preliminary

Santa Clara Valley Medical Center, San Jose

Jenelle Jindal, medicine-preliminary Maulik Shah, medicine-preliminary

Stanford University Programs Louis Salamone, general surgery

Sutter Medical Center of Santa Rosa Rachel Friedman, family medicine

UCLA Medical Center, Los Angeles Anne Ackerman, surgery-preliminary, urology

University of California, San Francisco Jessica Beard, general surgery Tina Dasgupta, radiation oncology Rasha Khoury, obstetrics and gynecology

Yunie Kim, internal medicine/primary Kiera Levine, psychiatry Maulik Shah, neurology Krishan Soni, internal medicine Michael Swetye, psychiatry James Troy, internal medicine Pavithra Venkat, obstetrics and gynecology

Connecticut

Greenwich Hospital Claudia Castiblanco, medicine-

preliminary



Griffin Hospital, Derby Louvonia Boone, medicine-preliminary

Hospital of Saint Raphael, New Haven Jennifer Dominguez, medicine-

preliminary

Keith Gipson, transitional Nandakumar Narayanan, medicinepreliminary

Karen Shoebotham, transitional Hannah Yu, medicine-preliminary

St. Vincent's Medical Center, Bridgeport Scott Kennedy, transitional

University of Connecticut Program,

Farmington Keith Gipson, anesthesiology Jeannine Ruby, general surgery Yale-New Haven Hospital

Mary Allison Arwady, medicine/ pediatrics

Eric Arzubi, psychiatry Erik Carlson, orthopaedic surgery Claudia Castiblanco, ophthalmology Douglas Davis, medicine/primarypreliminary, diagnostic radiology

Jennifer Dominguez, anesthesiology Ryan Hebert, surgery-preliminary, neurosurgery

Kristin Hoffmann, medicine/primary-

preliminary, dermatology Lily Horng, internal medicine Rasika Jayasekera, psychiatry Kimberly Johung, medicine-

preliminary, radiation oncology Rachel Laff, Internal medicine/primary Tamara Lazic, medicine/primary-

preliminary Nandakumar Narayanan, neurology David Peaper, clinical pathology Elizabeth Wahl, internal medicine/ primary

District of Columbia

Children's Nat'l Medical Center/ George Washington University Ephat Russcol, pediatrics

Uniformed Services University of the Health Sciences

Melissa Wollan, obstetrics and gynecology

Walter Reed Army Medical Center Amanda Sandoval, psychiatry Indy Wilkinson, anesthesiology Kimberly Schinnerer, medicine-

preliminary

Corinna Levine, left, shared the good news with classmate Zofia Piotrowska.



Florida

Jackson Memorial Hospital, Miami Gabriel Widi, neurosurgery-preliminary

Mount Sinai Medical Center of Florida Program, Miami Beach Roger Goldberg, medicine-preliminary

University of Miami Gabriel Widi, neurosurgery

University of Miami/Bascom Palmer Eye Institute Roger Goldberg, ophthalmology

Illinois

University of Chicago Medical Center Jason Griffith, internal medicine/ M.D. scientist

lowa

University of Iowa Hospitals and Clinics, Iowa City Paul Walker, otolaryngology

Maryland

Johns Hopkins Hospital, Baltimore Mohamad Bydon, surgery-

preliminary, neurosurgery Julia Marsh, internal medicine Kimberly Schinnerer, anesthesiology

Johns Hopkins University Alison Norris, social science postdoctoral fellow

Johns Hopkins University/Bayview Medical Center Elizabeth Houle, medicine-preliminary

Johns Hopkins University/Wilmer Eye Institute

Elizabeth Houle, ophthalmology

Massachusetts Brigham and Women's Hospital,

Boston

Candace Feldman, internal medicine/ primary Sarah Frasure, emergency medicine Sanaz Ghazal, obstetrics and gynecology Karl Laskowski, internal medicine Sean McBride, radiation oncology

Zofia Piotrowska, internal medicine Jason Roh, internal medicine Margaret Samuels-Kalow, emergency medicine

Massachusetts General Hospital, Boston

Argyro Caminis, psychiatry Sharmin Ghaznavi, psychiatry Ellen House, psychiatry Jenelle Jindal, neurology Ryan Kaple, internal medicine Jeffrey Winer, pediatrics

Massachusetts General Hospital/ Harvard Combined Program Dania Magri, orthopaedic surgery Andrew Simpson, orthopaedic surgery

Mount Auburn Hospital Program, Cambridge Karen Shoebotham, diagnostic radiology

Minnesota

Regions Hospital/HealthPartners Institute, St. Paul Timothy Sullivan, emergency medicine

Missouri

Barnes-Jewish Hospital, St. Louis Gregory Nelson, orthopaedic surgery

New York

Albert Einstein College of Medicine (Jacobi/Montefiore), Bronx Kurtland Ma, emergency medicine

Albert Einstein College/Montefiore Medical Center, Bronx Liza Goldman Huertas, family medicine

Hospital for Special Surgery/Cornell Medical Center, New York City Peter Fabricant, orthopaedic surgery

Memorial Sloan-Kettering Cancer Center, New York City Tina Dasgupta, transitional Carolyn Graeber, transitional Sophia Liu, transitional

Mount Sinai Hospital, New York City Leon Boudourakis, general surgery Lindsay McGuire, medicine-preliminary

New York-Presbyterian Hospital– Columbia University Medical Center, New York City Louvonia Boone, anesthesiology Cynthia Correll, medicine-preliminary, neurology Sophia Liu, anesthesiology Christopher Winterbottom, internal medicine Hannah Yu, anesthesiology

New York-Presbyterian Hospital– Weill Cornell Medical Center, New York City Scott Kennedy, diagnostic radiology Lindsay McGuire, dermatology Lori Spoozak, obstetrics and gynecology

New York University School of Medicine, New York City Benjamin Bowling, internal medicine Carolyn Graeber, ophthalmology Mark McRae, plastic surgery Kristina Zdanys, psychiatry

St. Luke's-Roosevelt Hospital Center Program Barbara Wexelman, general surgery BELOW LEFT Gene-Fu Liu and Julia Marsh, right, celebrated.

BELOW RIGHT Kristin Hoffman will stay in New Haven for a dermatology residency. BOTTOM Yunie Kim discussed the Match with faculty member Cyrus Kapadia.





Ohio Cleveland Clinic Foundation Al Makkouk, orthopaedic surgery

Pennsylvania Children's Hospital of Philadelphia Kevin Lau, pediatrics Tamara Miller, pediatrics

Drexel University College of Medicine, Philadelphia Abby Hochberg, medicinepreliminary, dermatology

Ashley Neal, pediatrics

Hospital of the University of Pennsylvania, Philadelphia Lu Anne Dinglasan, diagnostic radiology

Pennsylvania Hospital, Philadelphia Lu Anne Dinglasan, medicinepreliminary

University of Pittsburgh Medical Center

Misaki Kiguchi, vascular surgery Amy Meadows, pediatrics/psychiatryadult and child Danielle Smith, obstetrics and gynecology

Rhode Island Rhode Island Hospital/Brown University, Providence Alexander Diaz de Villalvilla, medicine/pediatrics

Roger Williams Medical Center Program, Providence Tamara Lazic, dermatology

Tennessee Vanderbilt University Medical Center Jennifer Giltnane, pathology

Washington Swedish Medical Center Program, Seattle Soledad Ayres, family medicine

University of Washington Affiliated Hospitals, Seattle Corinna Levine, otolaryngology/

research Natalya Lopushnyan, surgerypreliminary, urology



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Reunion 2008

The big news and main attraction of this year's alumni gathering was the university's new West Campus, which could transform research at Yale.



Dean Robert Alpern led alumni on a tour of Yale's new West Campus, a former pharmaceutical facility that straddles the neighboring towns of West Haven and Orange and that will provide the university with 1.5 million square feet of new office, storage and laboratory space.

This year's reunion was a jaw-dropping experience for the scores of alumni who toured Yale University's new West Campus during the weekend. On the three buses shuttling alumni to the 136-acre campus in neighboring West Haven and Orange and in the corridors of one of the site's research buildings, alumni marveled at the new space. its pristine laboratories and the low price. When Dean Robert J. Alpern, м.р., Ensign Professor of Medicine, led alumni down a hallway past a chemistry lab that seemed to stretch forever, the possibilities for research seemed equally endless.

After a brief tour of the lab and its 12-foot chemistry hoods followed by a lunch in the facility's cafeteria, Alpern described the process that led to the university's \$109 million purchase of the site and its 1.5 million square feet of office, storage and research space, as well as some of the medical school's plans for its use. "We don't see this as a site for classroom teaching," Alpern said, "but we do see this as a site for research, some of which will include student participation."

The first research program to be based at West Campus will be the new Center for High-Throughput Cell Biology, headed by the new chair of cell biology, James E. Rothman, PH.D. '71, the Fergus F. Wallace Professor of Biomedical Sciences. The center will focus on developing tools and techniques for analyzing the cellular functions of the 25,000 known proteincoding genes in the human genome.

West Campus, Alpern said, may also be a site for clinical use. Yale-New Haven Hospital sees potential for building an emergency room, and Yale Medical Group could open clinical practices at West Campus, which has parking for 3,000 cars. "For people coming up from southern Connecticut, the thing they hate most is the last 10 minutes, driving into New Haven and trying to find parking," Alpern said.

Bayer HealthCare, which had owned the site for decades, decided to close it down in 2006 after a corporate merger. The company put the property on the market hoping to sell it to another pharmaceutical firm, but the only bids came from developers interested in the land. "When it became clear that no pharmaceutical company was going to come into the bidding process ... they told us they would love to get a bid from us," Alpern said. "The developers were getting land. We were getting research buildings, office buildings and land. The biggest bonus is the time. If I convince [Yale President Richard C. Levin] that we need to start today on a new research building, it is a six-year time frame. ... We have gotten something that would have taken six years."

West Campus was also a central theme in Alpern's State of the School address earlier that day at the Association of Yale Alumni in Medicine's business meeting. "We want to establish programs of exceptional quality that greatly enrich science at Yale and outside of Yale," Alpern said, explaining the vision for the new campus. "This needs to transform science at Yale."

West Campus was not the only topic, however, in Alpern's discussion of the state of the school. The School of Medicine, he said, remains one of the best in the world. "It has become absolutely impossible to get into the School of Medicine. We get over 4,000 applications for 100 spaces," he said. "The top 1,000 applicants are indistinguishable, they are so fantastic."

Among the new educational initiatives is a program for clinical clerkships in global health, which relies on established and ongoing programs with universities and hospitals abroad. "We used to let students pick a place in Africa and go there," Alpern said. "Now we really try to have organized rotations."

The medical school is moving away from the traditional "see one, do one, teach one" methodology through the use of such computerized models that mimic the human body as SimMan, a portable manikin that allows students to practice emergency treatment techniques and decision-making skills. "It is completely real," Alpern said. "You see EKG, you see vital signs, you give medications. You don't know that the patient isn't real." The medical school has also adjusted its financial aid policy (see related story, page 7), in order to ease the burden on middleincome families.

The clinical practice, Alpern said, is the fastest-growing area of the medical school. The partnership with Yale-New Haven Hospital, he said, "has never been better." The new liver transplant program had performed 33 procedures since the summer of 2007; in September 2007 the program completed the first split-liver transplant in the state. "We have overnight become a center for liver transplants," he said.

At the alumni meeting that morning Christine A. Walsh, M.D. '73, a professor of clinical pediatrics at Albert Einstein College of Medicine in New York, received the Distinguished Alumni Service Award in recognition of her service to her profession, patients and family. "It is icing on the cake to receive an award for something you absolutely love to do," Walsh said.

Improved outcomes for autism

Diagnosing autism these days, said Fred R. Volkmar, M.D., director of the Yale Child Study Center, is something like filling out a form to diagnose deafness. "You'd say 'I want a hearing test!' ... We're trying to make the diagnosis [of autism] ... more like a hearing test."

Although researchers have found some genetic markers for autism, diagnosis is still a complex process requiring far more than a simple hearing exam. The current diagnostic gold standard requires the judgment of an experienced clinician who looks for certain behaviors in a child and discusses the child's developmental history with his or her caregiver. Most cases aren't diagnosed until the child is between the ages of 3 and 5; however, recent advances have allowed clinicians to diagnose the disorder in children as young as 2. Clinicians and researchers at Yale are now developing ways to spot autism even earlier.

Formal diagnostic criteria became available only in 1980, and research and interventions developed since then have led to improved outcomes. Autistic children now apply for college, Volkmar said—something unthinkable 25 years ago. "In a university setting," Volkmar joked, the odd social behaviors typical of people with autism "are often more easily tolerated and people can fit right in."

Volkmar and his colleague Ami Klin, PH.D., director of the Yale Autism Program, described new diagnostic techniques at this year's reunion symposium. The new approaches allow clinicians to deduce what a child is thinking by tracking what she looks at. Klin's team recently found that toddlers who were later diagnosed with autism, when shown a video of a woman speaking tenderly into the camera, pay attention mostly to her mouth or to background objects. Other children typically watch the woman's eyes.

The eye-tracking technology that led to this discovery has been central to research at the Child Study Center since 2000, when Warren Jones, now a graduate student in neuroscience, proposed its use to Klin. Using this technique, researchers found that autistic adults watch actors' mouths or background objects during emotional movie scenes rather than the actors' faces. Brain imaging studies confirmed that people with autism see human faces the way normal people see objects.

The youngest subjects of eye-tracking technology, though, are infants. The team created a video of a human figure rendered as a series of moving dots along with a spoken soundtrack; they then showed the video to babies. Infants later diagnosed with autism tended to look at both upright and upside-down figures, while normal babies preferred the upright figures. The autistic group, though, were more interested in



Ami Klin and Fred Volkmar (at lectern) described new techniques for studying autism at the reunion's scientific symposium.

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figures that move in time with the soundtrack. This preference for audiovisual synchrony may be part of the reason that autistic people watch lips so intently—they're drawn to the synchronous occurrence of lip movements and speech sounds. The team showed that mouth-looking exceeds eyelooking as early as 5 months of age in at-risk infants.

Volkmar and Klin hope that in the near future babies held on a parent's lap can watch a video while eye-tracking technology monitors their gaze and offers an early diagnosis of autism. But little research on effective treatments has been done in children under the age of 3. Klin told the audience that a task force for extending therapies to babies has been formed. "We need a rapidresponse system for the very young children who can't wait."

Telemedicine's global reach

At \$10,000 per hour for analog satellite time, said Ronald C. Merrell, M.D., the world's first telemedical surgery "was a little bit, well, unwieldy."

The former chair of surgery at Yale referred to a pioneering open-heart operation in Houston in 1965, when a satellite linkup connected legendary surgeon Michael E. DeBakey, M.D., to viewers in Geneva. More recently, a surgeon in New York performed the first fully remote surgery on a patient in France. The momentous event was underreported, said Merrell, because the press conference was scheduled for September 11, 2001.

Merrell, who left Yale in 1999 to become chair of surgery at Virginia Commonwealth University (vcu), discussed the past, present and future of telemedicine at the Yale Surgical Society Spring Reunion, which was held this year in his honor. He now leads the Medical Informatics and Technology Applications Consortium at vcu. Telemedicine, he said, is "the application of telecommunications and information science to support the delivery of health care at a distance."

Telemedicine is already with us in many ways, he said. Picture archiving and communication systems, now common, allow radiologists to diagnose patients from thousands of miles away. Preoperative clearance can also be done remotely, as Merrell and a team of surgeons demonstrated when they cleared the way for patients in the Dominican Republic to undergo surgery before the surgeons had arrived. A satellite dish installed on the roof of an outbuilding provided the link for low-bandwidth video.

In medical education, Merrell said, telemedicine can be as simple as Internet access in Kenya from solarpowered laptops, or as sophisticated as the class he once taught from the operating room for a group of medical students in Russia. "Education can be distributed in virtual reality in ways that really do work," Merrell said, adding that he hoped such techniques would reduce our "separation and alienation from the developing world." Telemedical techniques might one day beam top-quality medical education into medical classrooms around the world.

"I would make this integral to the training of medical students internationally," he said. "As long as it's interactive, I think we can do as well as we could in a classroom."



Former chair of surgery Ronald Merrell was honored at the Yale Surgical Society Spring Reunion. In his address, Merrell described telemedical techniques that bring medical education around the world.

A focus on ethics in public health

As Lawrence O. Gostin, J.D., associate dean and the O'Neill Professor of Global Health Law at the Georgetown University Law Center, surveys the health landscape around the world, he comes to an obvious yet troubling conclusion. "Rich countries just don't care enough," he said, calling the response of the United States and other affluent countries to health inequalities "limited and quite pathetic."

Gostin, the keynote speaker at the School of Public Health's Alumni Day symposium, said that government leaders need to pay closer attention to health threats in other parts of the world. "Infectious diseases don't respect national borders," he said, noting that health issues pose serious ramifications for international commerce, trade, tourism and government stability. "States with unhealthy populations provide a great opportunity to harbor terrorists." Even the CIA, he said, uses infant mortality as a marker of political stability.

While such headline-grabbing events as the recent China earthquake and the East Asian tsunami of December 2004 are typically followed by a "powerful humanitarian response," Gostin said that help to meet such basic necessities as sanitation, clean air and water, pest abatement and vaccines is more urgently needed in developing countries. "It's disarmingly simple and inexpensive," he said. "They don't need state-of-the-art facilities or foreign aid workers parachuting in to rescue them; they just need basic stuff they can run themselves."

Noting that governments currently exist in a state of "global health anarchy," Gostin proposed the creation of an international framework convention on global health modeled on the Kyoto Protocol, which raised the visibility of climate change as a global threat. The framework convention, an idea that is already being discussed by the World Health Organization and other international agencies, would convene key stakeholders for the purpose of addressing health disparities and developing global health solutions.

When it comes to health, "the poor suffer much more than the rich," Gostin said. "Health disparities are no less important than global warming and other issues of the times."

The panel that followed Gostin's talk also pursued the subject of ethics and public health. On the panel was Stewart D. Smith, M.A., M.P.H. '96, a former Navy officer, who served in the first Gulf War and was in the Pentagon on September 11. Since leaving the military, Smith has made a career as a consultant who helps organizations prepare for disaster. However, he has yet to see a company disaster plan that includes an ethics analysis. "Everybody assumes that ethics is common sense, that they intuitively know the right thing to do, and-guess what-they really don't. They need to be taught; and the time to do it is *before* disaster strikes," he said. For example, a recent government survey found that 73 percent of its employees would not come to work during a flu outbreak. Would it be ethical to require them to? "Get real," said Smith. "Ethics is real."



Curtis Patton presented posthumously the Award for Excellence in Public Health to the late Virginia Alexander. Her great-niece, Virginia Brown, and niece, Rae Alexander-Minter, accepted the award.

Smith was one of four panelists to discuss the importance of ethics in emergency planning and public health. Speaking from their own experiences which range from military action to anthrax attacks—the panelists made a strong case for ethics training in public health education and decision making.

James L. Hadler. м.р., FW '80. м.р.н. '82, who recently retired as chief of the infectious diseases section at the Connecticut Department of Public Health, often juggles benefits to the community and individual rights. (See related story, page 58.) He usually favors the welfare of the community "when the individual can't predictably be harmed." But determining the chances of harm isn't always easy. During a meningitis outbreak on college campuses just a few days before the end of a semester, for example, Hadler had to decide whether to vaccinate more than 12,000 students with jet-injector guns that carried a small risk of cross-contamination with bloodborne pathogens or with injections that would take much longer to administer, thereby putting students at risk of meningitis infections. After consulting with an ethicist and the Centers for Disease Control and Prevention, and researching different brands, Hadler authorized the use of jet-injector guns.

On a smaller scale, there are the problems of running an inner-city clinic. "Do we rob Peter to pay Paul?" asked Thomas J. Krause, M.P.H. '81. For Krause, that question isn't just hypothetical. Krause is chief operations officer at Southwest Community Health Center in Bridgeport, where most of his patients are self-pay or have Medicaid, and every year he faces budget cuts. He is responsible for delivering health care to poor people, many of them immigrants who have never encountered Western medicine. And he must maintain the morale of a staff that is hamstrung by scarcity and the difficulty of caring for this patient population. In the face of such pressures, it would be easy to think of ways to trim and skimp, Krause said. "But we never go there."

Bruce Jennings, M.A., a lecturer in ethics at the School of Public Health, explored the philosophical underpinnings of the others' real-world stories. The idea that society serves the individual and not the other way around, he said, sometimes "butts heads" with public health when officials must weigh an individual's liberty against the greater public good. Debates from the early days of AIDS provide an example. As the epidemic silently spread, public health officials pushed for greater tracking and surveillance of cases, while others argued that to do so would infringe on privacy rights. Since the AIDS era began, he said, "it has been impossible to take a purely libertarian [standpoint] and it has been impossible to be purely utilitarian." But, he added, "We have to figure out how to get respect for persons and liberty-and outcomes and health-together."

Awards and the state of the school

Dean Paul D. Cleary, PH.D., delivered good news to those gathered at Alumni Day 2008 at the New Haven Lawn Club—the School of Public Health has gone through a successful reaccreditation process. And, Cleary said, changes are in the works for the school, including a revamping of the global health program.



TOP Christine Walsh received the Distinguished Alumni Service Award, for her contributions to the school and the profession, from Dean Robert Alpern.

ABOVE Tobias Carling, Vikram Reddy and Walter Longo at the Yale Surgical Society Spring Reunion. "We stopped admitting students to global health last year," Cleary said. "We dissolved the division of global health and created a schoolwide global health program."

In addition, he said, Elizabeth H. Bradley, PH.D., professor of public health (health policy), is developing a global health leadership initiative that will bring practitioners from around the world to Yale. The school has also created an office of community health, led by Elaine O'Keefe, former head of the New Haven Health Department's AIDS division and former health director for the town of Stratford. The new office will oversee student internships, Cleary said. "We will move from a less-thanoptimal approach to a better-focused, more-managed program," he said.

The Association of Yale Alumni in Public Health (AYAPH) presented several awards this year.

Robert E. Steele, M.P.H. '71, PH.D. '75, M.DIV., received the Distinguished Alumni Award for his contributions to the school and the profession. Steele has been on the AYAPH board since 2001 and served as president from 2004 to 2007. He is a founder and benefactor of the Creed/Patton/Steele Endowed Scholarship Fund, which supports future public health professionals. "It is important to support the institutions that have supported us," Steele said as he accepted the award.

The Eric W. Mood New Professionals Award went to Keshia M. Pollack, M.P.H. '02, PH.D., who teaches at Johns Hopkins Bloomberg School of Public Health. She also works for a member of the Maryland General Assembly and advises a Baltimore community coalition seeking to alleviate childhood obesity.

The Award for Excellence in Public Health Practice was given posthumously to Virginia Alexander, M.D., M.P.H. '41. Alexander received her medical degree from Woman's College of Pennsylvania in 1925, but no Philadelphia hospital would accept Alexander, who was African-American, for training. Instead she completed her internship at Kansas City General Hospital, in Missouri, the designated hospital for people of color in that city. After receiving her public health degree from Yale, she became physician-in-charge of women students at Howard University in Washington, D.C. Her niece, Rae Alexander-Minter, ED.D., and great-niece, Virginia Brown, accepted the award on her behalf.

HIN CURIS

PHYSICIAN ASSOCIATE ALUMNI HOLD REUNION

About two dozen alumni of the Physician Associate Program gathered in June for their fourth annual reunion. The tradition started in 2005, as graduates from the program's 35 years reunited over dinner at the Graduate Club on Elm Street. With program director Mary L. Warner, PA-c (third from left), were, from left, Gary Spinner, PA-c '83; Kenneth Watkins, PA-c '98; and John Cassidy, PA-c '73.

1948

6oth Reunion

The 6oth reunion of the Class of 1948 was a great success. As of June this year 31 of the 55 of us who graduated in 1948 were still around, and 15 attended the reunion along with nine of the wives. They were a pretty vigorous bunch of 80-somethings.

Three of our five living women members were there. The prize for vigor has to go to Elizabeth Fuller Elsner, who spends the winter in Alaska where she is addicted to cross-country skiing. She had to take time off this past year to get a new hip but she is now back to her old sport. She spends the summer in Massachusetts and came down on Saturday morning with Nan Godley. Nan still does some volunteer work at Harvard. Sylvia Preston Griffiths also does volunteer work at Columbia.

The prize for the longest trip goes to Al and Ruth Fisk who came from California. They live in the Sonoma valley and until recently had a small vineyard. They also won a gold medal in 2003 at the Cal State Fair for their pinot noir. They have now given up the vineyard and keep busy with duplicate bridge, gardening and leading environmental walks. Next longest was Jock Bishop, who is retired from an academic career at Minnesota in internal medicine and research in the physiology and biochemistry of diabetes. He now pursues a hobby in creating rustic furniture from buckhorn wood. In listing our longer travelers I overlooked Dick Buker who is the last member of our class still seeing patients. He is the county health officer of Chester, Mont., and is in charge of disaster planning for his area. He attended with Candace Chang.

Bob and Mary **Lempke** joined the group on Friday from Indiana. The OR at the Richard L. Roudebush Indianapolis VA Medical Center was named in Bob's honor. He was chief of surgery there for many years. He has taken up oil paintinglandscapes and some portraits and has had a showing of his works in Indianapolis. **Dave** and Kayoke **Morton** came from Pueblo, Colo. They have been doing a lot of traveling, including trips to Japan to see Kayoke's relatives.

Bud and Esther Rowland, Jack and Ann Strominger and Paul Talalay came from Columbia. Harvard and Johns Hopkins respectively. I mention them together because they probably represent the most successful of our academicians. Paul is the John Jacob Abel Professor of Molecular Pharmacology at Hopkins. He is widely known for his studies of vegetables like broccoli that induce protective enzymes in the body and help prevent cancer. In 2005 he was awarded the prestigious Linus Pauling Award in recognition of his work. Jack is a professor at the Dana Farber institute at Harvard. He has studied histo-compatibility in man and other vertebrates leading to the understanding of mechanisms of immune recognition. In 1999 he received the Japan Prize, the largest monetary reward for scientific investigation. Bud was chief of the department of neurology at Columbia's Neurological Institute and was widely known for his work on stroke.

Paul and Betty Goldstein, Paul and Margaret Koehler, and Dick Richardson represent our clinicians who remained in the Northeast. Paul is the only member of the class who remained in New Haven and has been an anchor for returning alumni. He now spends winters in Florida. When he is in New Haven he spends one day a week in his clinic. Dick Peterson is now retired. He drove down from Southbury, Conn., with his daughter Melanie Barry. Paul and Margaret drove down from Newbury, N.H. Paul served us for 50 years as class secretary. He's still pretty active despite acquiring four artificial joints.

During the spring I contacted almost everyone in our class. I'd like to mention three of our achievers who couldn't come. They are **Herold Griffith**, **Tom Frei** and Betty McCleary Hamburg. Herold spent eight years as chief of plastic surgery at the University of Illinois medical school. He was made an honorary member of British Association of Plastic Reconstructive and Aesthetic Surgeons, of which there are only eight in the United States. Tom is the Richard and Susan Smith Distinguished Professor of Medicine at Harvard and a member of the Dana Farber Cancer Institute. In 1972 he was given the Albert Lasker Medical Research Award for demonstrating that a combination of chemotherapeutic agents could result in long-term survival and even cures in some leukemias and lymphomas. This award is often a prelude to the Nobel Prize. Betty reports having two careers, first as a professor at Harvard and then as the first director of child psychiatry at The Mount Sinai Medical Center in New York City. After retiring from Mount Sinai, she began a second career as president of the William T. Grant Foundation. Herold couldn't come because his wife is so frail. Tom couldn't make it for health reasons. Betty thought she could come in on Saturday but something must have interfered. Looking forward to seeing all

of you on our 65th. Ben Rush

1953

55th Reunion

Our 55th class reunion welcomed 10 of our members, who had lively discussions in many venues. Two of our married sets, Ed and Rhoda Powsner and Ora and Howie Smith, added greatly to the pleasure of the weekend. Attending some of the reunion activities were Claude Bloch, Fred Lane and José Ramírez-Rivera. Tom Gentsch was accompanied by wife Betty. Hyla and Bob Melnick had to leave early Sunday to welcome a new grandchild who had arrived on Saturday. Maureen was with Hal Bornstein. Many of our regular attendees had excused absences for a variety of reasons from knee replacement











to family conflicts. Excellent weather enhanced the reunion program, especially the tour of Yale's new West Campus.

Harold D. Bornstein

1958

50th Reunion

Thirty-two members of our class of 72 graduates were in attendance. Many with their wives or significant others were there to partake of the festivities. George and Anne Aghajanian, Joe and Ann Angelo, John and Trudy Arnot, Gerry and Ann Burrow, Dave and Helen Carlson, Joe Cillo and Tina Callahan, John and Sheila Creatura, Bob and Ellen Donohue, Larry and Reggie Dubin, Don and Helen Duncan, Michael and Liz Fishman, Marcia Kraft Goin, Bill and Sue Gould. Stan and Debbie Harris, Ernie Hartmann, Dick Hinckley, Mike and Jean Kashgarian, Jay and Barbara Kislak, Ted and Dora Lieberman, Tom and Karen Mauro, Bill McClanahan and Anne Bourne, Andy and Lois McGowan, Richard and Eva Miller, Al and Judie Muggia, Bob Neuwirth, Carol Phillips, Bill and Dorothy Radcliffe, Paul and Sandra Rudnick, Bruce Sklarew and Margaret Meyer, Ray and Maria Turner, Jack and Pauli Wood. We missed Bill Schlaepfer who could not attend and were sorry to hear that Chuck Kashima was not doing well. Our Friday night class dinner was held at the old Fulton Mansion on Deepwood Drive. We were fortunate to enlist the Union League Café as our caterers since they produce the best French cuisine in Connecticut. Dean Robert Alpern joined us and assured us that the Yale system, although somewhat modified by external influences, is still alive and well and is attracting the very best students. We started dinner with a toast to honor the 10 members of our graduating class who have passed on over the years. John Carlston, Jake Gallagher, Dick Gershon, Jim Greenwald, Ken Jimenez, Mike Lotz, Pat McKegney, Al Phillips, Dave Pugh, Tom Shea, and Bob Wroblewski, Alumni

Day began with a symposium on autism that fascinated and enthralled all who attended. The afternoon was occupied by some with a visit to the new West Campus, where new programs in biotechnology, chemistry, physics, environmental sciences and art preservation will take place, while others had some moments of nostalgia by having pizza at Pepe's on Wooster Street. The weekend ended with dinner with the Friends of the 50th at the Graduate Club, where old friendships were renewed. Mike McCabe did not attend and is still surfing in Hawaii and sends this message "I miss all of you guys. But I love surfing my Hawaiian waves. So, come visit me in Hawaii!"

Mike Kashgarian Gerry Burrow

1963

45th Reunion

Eleven members of the Class of 1963, many accompanied by their spouses, made their way back to the mother ship for the 45th Reunion. Sending regrets but unable to attend because of illnesses, prior commitments, unavoidable conflicts or intractable lethargy were Wayne Brenckman, Bill Friedewald, Bill Lehmann, Bob Mueller, Bob Grummon, Seth Weingarten, Steve Joseph, Lee Tainer, Peter Gregory, Judy Davis, John Mahoney, Rick Back, Dudley Danoff, Allen Flaxman, Ben Harris, Pete Tishler, Larry Tremonti, Jim Dalsimer, Gordon Cohen, John Conte, Bill Porter and Gene Profant. Many commitments were offered for attendance at our 50th in 2013.

Our small but very congenial and talkative group lingered through extensive conversation and reminiscing at Friday's clambake and a marvelous Saturday dinner at the Q-Club. **Art Ackerman**, who has been bringing Western medicine to the backwaters of developing countries over many decades, continues to do so, most recently in Africa (Tanzania and Rwanda) and the Caribbean (Antigua). Colonel **Craig Llewellyn**, fully retired from his longtime Army career, splits his time between Florida and Vermont, while teaching and assisting in the establishment of emergency preparedness teams and procedures at universities. Sheldon Pinnell, a Duke faculty guy since 1973 and self-confessed workaholic, sold his SkinCeuticals Company (for which he developed research-based sunscreen and antioxidant skin protection and restoration products) to L'Oréal, and continues to spend full days in his lab at Durham, having a good time. Dave Fulmer, on the other hand, has his good times at the front end of a fishing rod. Back at the turn of the millennium, Dave decided that he had had enough of managed care and other regulatory baloney and would retire from his internal medicine practice in Princeton, N.J., and start enjoying his seven grandkids. Alex Gaudio continues his full-time retinal disease practice in Hartford, Conn., now with his son, Paul, and spends one day every week maintaining his academic connection at Mass Eye and Ear in Boston. Hal Kaplan finally retired from his gastroenterology practice in July 2007, but continues in his "part-time" medical affairs consulting slot at his old hospital in Meriden, Conn., while finding more time to enjoy his 10 (and still counting?) grandchildren. Mike Fessel, also still hanging out in the New Haven area, practices internal medicine, and, along with Hal, enjoys a clinical appointment to the med school faculty, trying to teach the art of effective communication with patients and family. Andy Edin continues his active internal medicine practice in Minnesota. Part of a large multi-specialty group, he now arranges his patient schedule on his own terms, allowing him time to enjoy his longtime hobby of hunting in Minnesota (these days, without shooting), as well as in any number of remote locations. Alan Shapiro remains happy in an active urology practice in Tinseltown, Helen Walsh, long since moved on from a career in anesthesia to one in psychiatry,

is quite active and happy with a part-time Massachusetts practice limited to geriatric psychiatry. Also still engaged in a part-time psychiatric practice is Jay **Pomeranz**, who in his free time wields a very competitive tennis racquet in Springfield, Mass.

Twenty-nine classmates contributed to the 45th Reunion Booklet, providing a variety of long and short glimpses of their personal lives, with fascinating details beyond the limited scope of this article. Copies will be distributed by mail to all members of the Class of 1963. This mailing will be the first phase of an intensive campaign to encourage maximum attendance at our 50th reunion, scheduled for June 7–8, 2013. SAVE THE DATES!

Harold Kaplan

1968

40th Reunion

Seventeen members of the Class of 1968 came to New Haven for our 40th reunion. Elizabeth Short provided the star attraction with the 2008 edition of the Class Roster, a 139-page summary of the class that will be mailed to all who did not attend. Grace Jordison Boxer came with husband Larry from Michigan. Bob Dillard, who came with wife Laura, reminded us of his passions for treating sick babies and for fly fishing. Alan Finesilver, who came with wife Cindy, is also an avid fly fisherman (Wisconsin and Montana) and works as a volunteer to help find housing for homeless people. Bill Flynn Jr. is still working as a general surgeon with no intention of retiring any time soon. Gil Grand revels in his "perpetual immaturity." Len Grauer, who came with wife Betsy, was "delighted to see everyone." Ralph Greco came with wife Irene Wapnir. Peter Jokl was excused from the fête due to aortic valve surgery a few weeks earlier. Marc Lippman was happy "just to be here." Frank Lucente, who came with partner Stephen Saikin, tells us he is now enjoying "minimal work." Allen McCutchan and wife Emily are anticipating

semiretirement soon. Richard Morehead invites us all to Santa Fe. N.M., for next year's West Coast reunion-a necessary location due to global warming (i.e., no more West Coast). Jim Ogilvie is happy to "see a happy and productive Class of '68. We're not done vet!" Jerry Rauch and wife Nancy have been traveling internationally, rebuilding their house and volunteering at an animal shelter. Peter Kirkpatrick says this event brings back good memories. And Chuck Post has been semiretired for 8 years, sailing along the East Coast and the Caribbean, doing surgery in the Third World and bicycling in various countries.

Donald Lyman

1973 35th reunion

Among those who made the pilgrimage were Marv Chassin and wife Barbara, now in Phoenix, where Mary practices oncology. Marvin Miller is the class geneticist; he came from Dayton, Ohio, with wife and children. Sesh Cole and wife Pat came from St. Louis. where Sesh is in pediatrics at Washington University. They left the next day for Dartmouth's graduation. John Brown has retired from his surgical practice in Vancouver, Washington, and spends time in Mexico and Florida; he noted that John Jr. has presented him with grandchildren. Chris (Kull) Walsh arrived from New York with husband Sean. Chris is a pediatric cardiologist at Einstein and has a daughter in her own training program. Harry Romanowitz and wife Sheila drove up from Stamford, Conn., where Harry practices pediatrics. Doug Maddox and wife Kathryn flew in from Atlanta, where Doug is ENT chair at Emory.

On Saturday, Joe Eichenbaum, who practices ophthalmology at Mt. Sinai, and wife Ingrid joined us. Randy Zusman came from Boston; he has been at Mass. General since graduation. Tom Sweeney and Jim Sullivan were both in attendance, representing surgery and medicine in the New Haven community. **Rick** Young attended, fresh from his third tour of duty in Iraq. **Rick** is a pediatric neurologist and chair of pediatrics at the Hospital of Saint Raphael in New Haven. **Neil Handel** attended by phone, unable to make it from Los Angeles where he is a plastic surgeon and the proud father of three young children. I am a gastroenterologist in Dallas, run a colon cancer research laboratory, and still work on my medical school thesis.

We swapped tales about family and professional activities, tried to exchange information about those who weren't there, and made up what we didn't know for certain. We have produced two deans (Lee Goldman at Columbia and Dave Bailey at UC Irvine); several department chairs (George Lister in pediatrics at Southwestern Medical Center, Bob Buchholz, who just stepped down from orthopaedics at Southwestern. Jerry Rosenbaum in psychiatry at Mass. General, and probably

more); and many division chiefs and other academic leaders. We look forward to seeing more of you at future reunions.

Richard Boland

1978

30th Reunion

The Class of 1978 reconvened in New Haven this June for their 30th reunion. Sightings included Rich Baron, Duke and Claudia Cameron. Howard Chase and Claudia McNamara, Stuart and Amy Forman. Bob Gelfand and Susan Boulware, Ken Lee and Ruth Daniel, Yvette Piovanetti and Jose Martinez, Barb and Jordan Pober, Seth Powsner and Elizabeth Yen, Mike Rogawski, Bern Shen, Tom Smith and Joann Bodurtha, Marcia Wade and David Officer, John Wagner and Julie Budd, Jonathan Weinberg, and Susan Wong. Dean Alpern joined our class for dinner at the Graduate Club, either because of our illustrious record of charitable giving to Yale or our legacy of mischief ... you decide. It was a heartwarming and spirited evening. Those not in attendance were missed but also well represented in embarrassing vignettes. Remember this when you consider your plans to attend the 35th! Seth and I will get to work on a class survey to provide a little more detail on everyone's lives. Have a great summer. **Duke Cameron**

Seth Powsner

1983

25th Reunion

"Spectacular" describes our reunion. As we gathered on Harkness lawn, at the 333 Cedar St. rotunda, and in the Historical Library, it seemed as though just vesterday we were students.

Attendees included: Mark Boytim and Anne Boytim, Nancy Crocker, Dianne Edgar, Gerri Goodman, Linda Grais and John Freund, Tammy Harris, Rob Homer, Ana Lamas, Judy Melin, Elizabeth Nolan, David Norton, Dan Oren and Jeanette Kuvin Oren, Alan Reznik and Elizabeth Reznik, David Schwartz, Susan Seward and David Seward, Steven Sockin and Susan Sockin, Michael Silverberg, Michael Tom.

Among us are expert clinicians, educators, chiefs, chairs, partners, directors, trustees, researchers and administrators throughout the country. We discussed our residencies, fellowship training, current or prior practice experiences in allergy (Ana, Steve), ENT (Mike T.), ER Med (Elizabeth), ophthalmology (Gerri), orthopaedics (Alan, Mark), primary care specialties (Tammy-FP; Judy, Sue-IM; Dave N., Nancy-pedi). We talked of teaching, research and practice at Yale and in New Haven (Alan, Dan, Rob). We talked of clinical leadership roles in anesthesia (Dave S., Mike S.), of management/VC work in life sciences (Linda), in pharmaceutical research (Dan), of health care administration and policy work (Dave N., Judy, Nancy et al). Most talked of educating medical students and residents (Ana, Dan, Dave S., Gerri, Judy, Rob, Sue et al.).











Our dinner on a sunny summer day at Sage's, formerly Chart House, was the ideal setting for our class photo on the ocean deck. We reviewed **Alan's** copy of our Class Yearbook, **Judy's** copy of our first-year Facesheet, and were proud to learn that it's our class that revived the Yearbook tradition at the School of Medicine.

Other classmates heard from recently include Alan Bloom (ophthalmology), April Hang-Miller (rheumatology), David Helfgott (ID), and Eric Winer (oncology). Tina Young Pouissant and Valerie Stone led the establishment of the memorial fund honoring Yvedt Matory, M.D. '81. We thank Michael Tom, for his leadership role in the Yale Tomorrow School of Medicine alumni fund campaign, our reunion gift volunteers David Schwartz and Eric Winer, and reunion co-chair David Helfgott. We also extend our thanks to Joan Peck of the Association of Yale Alumni in Medicine for organizing our reunion, and to Mary Meehan, director of alumni affairs, and Claire Bessinger of Yale Medicine.

For classmates not here for the reunion, know we talked of your research advances, publications, teaching, leadership, and outstanding care you provide. When we next convene, we'll again prove accurate the refrain from our fourth-year show theme song, that we're "one singular sensation, Yale Med Class of '83." We'll be holding a place for each classmate at our next reunion. Do join us.

Judy Melin

1988

20th Reunion

It is hard to believe that it has been 20 years since we left New Haven, especially since everyone who attended looked unchanged from our medical school days. Five of us took a break from chauffeuring our children to their various activities and returned for this year's reunion.

Dave Chelmow arrived for the Saturday night dinner. He is the director of the ob/gyn residency program and the IRB chair at Tufts Medical Center in Boston. He and wife Fay, a hospice nurse, live in Newton, Mass. They have two children, Ben, 15, and Jenny, 11.

Nicole Davis and Alex Vukasin also attended the Saturday night dinner after driving up from Princeton, N.J. Nicole is a gynecologist in solo private practice and Alex is a urologist in a group practice. They have two children, Gabrielle, 16, and Alex, 13.

Irene Freeman attended most of the reunion festivities. She is a pediatrician in a group practice in Chicago. She lives with husband Bob McDonald, an economist at Northwestern University, in Evanston, III. They have three children, Claire, 15, David, 13, and Henry, 11.

Rhonda Karol attended the Saturday night dinner with husband Gordon Berger, a managing director of the Bank of New York Mellon (and a very good sport as he was the only non-alum and non-physician present). She continues working as a dermatologist in Forest Hills, N.Y., in the solo private practice she started 13 years ago. They live in Roslyn, N.Y., with their two children, Elizabeth, 13, and William, 10.

We reminisced about absent classmates and exchanged stories about our last sightings of various class members. We also very much missed **Martha Brochin**, who passed away since our last reunion. We hope that more of you will return to New Haven for our next reunion.

Rhonda Karol

1998

10th Reunion

The Class of 1998 set another reunion attendance record, this time for our 10th. Friday night brought the traditional clambake and overtired children. Saturday was filled with official Yale lectures and touring, capped off by a dinner at the New Haven Lawn Club with dancing to the DJ'ed music of **Richard Lyn-Cook** and his perennial roadie/sidekick, **Steven** **Williams**. Along the way we got updates from many of our classmates who were there.

Senai Asefaw lives in New Haven, where he works as a hospitalist at Yale-New Haven Hospital and does part-time consulting work. Kristen Aversa lives with her husband and children in Woodbridge, Conn., and continues to practice ob-gyn locally. Tamar Braverman and husband Michael brought their daughters Yael and Talya on Friday night. Tamar is an internist in Branford, Conn. Sydney Butts lives in Syracuse, N.Y., where she works as an ENT surgeon and volunteers her time reconstructing the faces of domestic violence victims. Kent and Shelley Chou flew in from Phoenix, where Kent is an orthopaedic surgeon.

Pediatricians Dan Coghlin and Barb McGee brought children Molly and Henry, who look like clones of their parents. Dan and Barb work in the same practice in Rhode Island. Psychiatrist Caroline Dumont lives with psychiatrist husband Brian Tobin and their three mentally healthy children in the New Haven area. Lawrence (Lori) Etter is a dermatologist in Durham, N.C. Husband Jeff Welty and daughter Caroline were barely recognizable beneath layers of sunscreen, hats, and longsleeved shirts. ENT Mark Homicz and Pam Loman came in from California wine country, where they live with their two children. Russ Huang is married, lives in New York and is a spine surgeon. Unfortunately, he has not had much time to play guitar, perhaps explaining the absence of class band Haploid Floyd at our reunion. Or Scott Floyd, for that matter, who wasn't at the reunion but who is a radiation oncologist in Boston.

One of our longest-in-training classmates, neurosurgeon Hahnah Kasowski and husband Robert Seminara live in New York with their son Nathaniel. Lisa Lipschitz practices obstetrics and gynecology in San Diego, where she lives with husband Steve Montal and their two children. Rich Lyn-Cook treats adults and kids, he spins tunes as a DJ, and he can impersonate any human born in the 19th or 20th centuries! The versatile **Rich** lives in Houston with his wife Monica, who is a surgeon but was too busy operating to join us.

After several years on faculty as a hospitalist at the University of Vermont, Ursula McVeigh recently moved to Boston to start a palliative care fellowship. Matt Mealiffe works as the director of clinical research at Perlegen Sciences in the South Bay. Ali Portnoy lives in Villanova, Penn., with husband Raphael Crawford; Ali works for GlaxoSmithKline as medical director of early phase clinical drug development in infectious disease. Ruth Potee lives in western Massachusetts with her husband Steve Martin and three kids; Ruth commutes once weekly to Boston, where she is on the family practice faculty at Boston Medical Center. Ruth is probably our only classmate who still sleeps in a call room once a week. Paul Pottinger lives in Seattle with wife Julie and children Zoe and Matthew. Paul is an infectious disease specialist, especially now that he has two children. Nikki Rabidou and her husband have a new baby boy; Nikki practices rheumatology in Torrington, Conn.

Greg Raskin lives in New York City and works at Alliance-Bernstein. Greg occasionally practices medicine on his wife Jackie Weiss and on his children Daphne and Morris.

Lisa Gale Suter, husband Lindsay and children Fenn and Halvor live near Yale, where Lisa is on faculty in rheumatology. They still have a sluice gate. Kimara Targoff and Josh live in New York with their three children. Kim is an instructor at Columbia in pediatric cardiology, and is also doing research on the regulation of cardiac development. Meena Thayu and husband Eric Keuffel have a year-old daughter Anna and live in Philadelphia, where Meena is a pediatric gastroenterologist at the Children's Hospital of Philadelphia. Ricky Torres isn't even in our class, but he gamely

showed up on Saturday night and danced some salsa. He's on faculty at Yale. **Sus Waikar** is a nephrologist at the Brigham in Boston and lives with his wife and kids in Brookline, Mass.

Steven Williams is a plastic surgeon in San Ramon, Calif., where he lives with his wife. Steve occasionally goes to Honduras on medical missions. Ashley Wivel lives with son Jackson in Philadelphia, where she works for GlaxoSmithKline as a pharmacovigilance specialist. Say that 10 times fast!

Lori Etter

2003

5th Reunion

If there had been one thing the 20 of us in attendance agreed upon, it was that everyone looked the same and no one seemed to have changed a bit. On the other hand, words cannot adequately capture all we have been through since graduating, so I will not attempt the impossible. Instead here are brief updates on those who made it to the reunion:

Severine Chavel Greenspan is finishing her dermatology residency at Yale and will begin private practice in Stamford, Conn., while remaining a volunteer attending at Yale. Severine and husband Mike have a 10month-old girl—Sophie! Mike Greenspan, one of several "Yale lifers" in attendance, is finishing his psych residency after winning the "world's strongest man competition." He will pursue a forensics fellowship at Yale, of all places.

Sean Christensen is beginning a four-year derm residency at Yale and proudly acknowledges his and Elin's official status as "lifers." Elin Lisska Christensen is now a partner in an internal medicine private practice in Madison, Conn. Elin and Sean just bought a house in Guilford. They are also celebrating their second wedding anniversary.

Doug Davis has "finally" graduated from the M.D./PH.D. program and is beginning his intern year in Yale's primary care internal medicine program.

Nataliya Uboha is beginning her second year of an internal medicine residency at Yale. She and husband Doug have bought a home in New Haven.

Danny Kanada had "two more weeks" of Yale radiology residency on reunion day. He's headed to UCSF for a crosssectional fellowship.

Pramita Kuruvilla is in the San Francisco Bay Area working as a hospitalist and teaching family medicine residents at Contra Costa Regional Medical Center.

Matt Goldenberg is an emergency psych attending and consultant/liaison at Dartmouth. He is contemplating focusing on refugee mental health and forecasts "liberation" in the near future.

Namita Seth Mohta lives in Cambridge, Mass., with husband Vinay and 10-month-old daughter Aanika. She is a clinical strategy consultant at Partners Health Care and a hospitalist at Brigham and Women's Hospital.

Kyeen Mesesan Andersson met husband Richard during her three years in South Africa completing her M.D./PH.D. She is now starting a postdoc at Yale.

Ada Emuwa, a family medicine physician, is moving with | husband Chi to Nashville, Tenn., and will practice in United Neighborhoods-Health Service Core Clinics for the underserved.

Satish Nagula finished an IM residency at Penn and is now living in NYC with wife Shreya, where he is completing his final year of a GI fellowship at Memorial Sloan-Kettering.

Marta Rivera is a hospitalist at Yale-New Haven Hospital after enjoying a highly recommended seven-month primary care stint in Hawaii post-residency. She has accepted a position in primary care in Virginia Beach, Va.

Dave Ross is finishing his third year in the Yale adult psychneuroscience research training program, where he continues researching his passion—music and the brain. **Rebecca Seekamp** is excitedly moving from Boston, where she is a practicing family doc, to San Francisco, where she will become a clinician-educator in Stanford's family medicine department.

Joahd Toure was found moonlighting in the Yale-New Haven MICU. He is finishing up a Robert Wood Johnson Clinical Scholars fellowship, moving to "the city" for a health care consulting position and still marveling at the recent purchase of a washer and dryer with wife Viviana.

Sunny Ramchandani is now a primary care internist with the U.S. Navy in Bethesda, Md. He is looking forward to seeing his fellow classmates at the next reunion!

Susan Rushing worked as an attorney before returning to medicine. She has two years left in psychiatry training at U Penn, where she assists with health law lectures at the med and law schools. She and husband Karl Richter have two children, Elizabeth, age 2, and Kaitlyn, age 2 months.

As for me, I am working on childhood obesity prevention as a special assistant to the president of the Robert Wood Johnson Foundation and as an obesity medicine consultant to Harvard Health Publications. I dream of resuming clinical work in obesity treatment and lifestyle medicine in the Promised Land (San Francisco).

Our goal is to have the entire class show up for the 10-year reunion. In the meantime, join our soon-to-be-created Facebook group to keep in touch and share news of the many bundles of joy brought into the world thus far as well as other life transitions.

Mark Berman













James Hadler began his career as a physician, but switched to public health. He retired recently after almost 25 years as Connecticut's state epidemiologist and chief of the state health department's Section of Infectious Diseases.

A career fighting infectious disease

Physician and Connecticut state epidemiologist James Hadler sees the public as his patient.

James L. Hadler, M.D., FW '80, M.P.H. '82, said that his relatives, many of whom are physicians, sometimes tease him for not working at the bedside. "They ask me, 'When are you going to be a *real* doctor?'" But, he said laughingly, "The public is my patient."

Hadler, who retired in June after almost 25 years as Connecticut's state epidemiologist and chief of the state health department's Section of Infectious Diseases, has steered the state through a plethora of public health crises, from AIDS to Lyme disease to anthrax. Although he started his career as a physician while working on the Navajo reservation for the Indian Health Service and the Centers for Disease Control (CDC), Hadler found he liked looking at health from the perspective of populations. The experience, he said, "sold me on a career in public health."

He came to the state health department in 1984, just as the AIDS epidemic was picking up speed. For the first four or five years, "HIV became my life." High-profile debates kept him in the public eye. For example, Connecticut had one of the first cases of a schoolaged child with AIDS, and under national media attention, Hadler developed safety guidelines to allow the child to return to school.

The mid-1990s saw a dramatic shift in emphasis after the Institute of Medicine published a paper stating that the country was unprepared to combat emerging infectious diseases. In 1995, the Emerging Infections Program, affiliated with the CDC, was established in partnership with the state health department and the Yale School of Public Health. It was soon busy with outbreaks of Eastern equine encephalitis and West Nile virus and the re-emergence of the then rare tick-borne diseases babesiosis and ehrlichiosis.

After September 11, 2001, bioterrorism preparedness became a priority. Hadler was on the front lines during that year's anthrax attacks (he still attends an annual symposium in honor of victim Ottilie Lundgren, a Connecticut resident and one of five people who died from exposure to anthrax), and later faced a crisis of conscience when he was instructed to prepare mass smallpox vaccinations prior to the invasion of Iraq, which he strongly opposed. Reasoning that to do so might embolden the Bush administration's threat to invade, he considered resigning. In the end, he decided that to quit or go on strike would not stop the war, and chose to stay, "although uneasily."

While in office, Hadler also oversaw an increase in childhood vaccinations against preventable diseases, the elimination of race-based disparities in childhood vaccination rates and the reduction of the rates of tuberculosis and several sexually transmitted diseases.

Hadler said that what has motivated him, in large part, is the combination of Connecticut's small size and its great population diversity. Its problems come in manageable "little packets." "New Haven has its down-and-out

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side, Hartford does, but ... they're all small compared to New York or Chicago," he said. "To me, [Connecticut] is a perfect laboratory to try to take on the challenges of diversity and health disparities."

Hadler grew up in Bethesda, Md., where his father worked as a naval architect and international consultant. The family hosted exchange students and had friends from other countries, and Hadler says those experiences—and his stint in Pakistan as an exchange student—gave him and his three siblings a global perspective.

He attended McGill University in Montreal, then went to Columbia University's College of Physicians and Surgeons. After an internship at Roosevelt Hospital in Manhattan, Hadler joined the Indian Health Service in a position supported by the CDC as a tuberculosis control officer. He completed his residency at Waterbury Hospital in Connecticut, did an infectious diseases fellowship at Yale-New Haven Hospital and then earned an м.р.н. Finally, he and his wife and two children spent a year in China as part of a School of Medicine exchange with Hunan Medical College. He began as Connecticut's state epidemiologist the following year.

The job, he said, has allowed him to combine diverse interests and to work with people from all walks of life. "Public health is dynamic," he said. "I love that aspect of the job."

Hadler lives in New Haven with his wife, Alice, who speaks several languages and whose experiences with adult education on the Navajo reservation with her husband grew into a teaching career; she is now an associate dean at Wesleyan. They have three grown children.

Hadler plans to work as a public health consultant to the state and to New York City. He will also write scientific papers, deliver talks and continue to teach at the School of Public Health.

—Jenny Blair

A primary care physician finds peace of mind in concierge medicine

On a typical day two years ago, Steven Fugaro, M.D. '81, saw a patient in his solo primary care practice every 10 to 15 minutes. Onerous paperwork and economic difficulties made it hard for the San Francisco-based physician to provide the quality of care he felt his 3,000 patients deserved. "I was becoming increasingly dissatisfied with what I was doing," he said, "although I was probably too busy to be reflective of it at that point."

Then MD², a concierge medicine group, based in Bellevue, Wash., approached him. Would he like to join them as a concierge physician and gain the time and resources to provide extraordinary care for a small number of patients? His decision to do so changed his life and made him part of a controversial trend in primary care.

Fugaro had opened a private practice after an internal medicine residency at the University of California, San Francisco, and eight years in academic medicine. Although he loved primary care, physicians in that field are under tremendous pressure to see patients in great numbers-time is tight, reimbursement rates are stagnant and preventive care must take a back seat to immediate problems. Few medical students choose the field, and many weary primary care physicians are retiring early or taking jobs in industry or administration. These doctors are in short supply.

Enter concierge medicine. In this model, introduced in 1996 by MD² founder Howard Maron, M.D., patients

Alumni FACES

Steven Fugaro traded a solo primary care practice for a career in concierge medicine.



pay a yearly fee ranging from \$15,000 for an individual to \$25,000 for a family of four. In return, physicians make themselves readily available, offering prompt appointments, house calls and other extras.

Critics of the practice, also known as "boutique medicine" or "retainerbased medicine," call it unethical. The retainer is beyond the means of many people and because concierge physicians care for fewer patients than other primary care doctors, the practice increases colleagues' burdens and may endanger access to care. But many concierge doctors say that they would have quit practicing altogether if not for this option. Fugaro agonized for months over his decision. "I was worried about what my colleagues would think. I was worried about ... leaving patients. I wondered if I would be intellectually stimulated," he said. "On the plus side [was] being able ... to have basically unlimited time with

[patients], to be able to care for them in a very holistic way and to have balance back in my life." For Fugaro that meant more time for such pursuits as mountain biking and spending time with his wife of 22 years and their son, who studies theater at Northwestern University.

In 2007, Fugaro arranged for the patients in his primary care practice to be cared for by a successor, Allan Treadwell, M.D., relinquishing the practice free of charge. Then Fugaro joined MD².

He cares for just 50 families now, and on a typical day sees or speaks to six to 10 of his patients. The office does many of its own tests, with results available on the spot. He makes regular house calls. Many of his patients have complex medical conditions and he is better able to anticipate problems before they arise. "I was juggling so many things before," Fugaro said, "it was clearly possible for something to fall through the cracks, and that's far less likely now." He also accompanies patients to specialty appointments and the ER, and enjoys learning from subspecialty colleagues at such times, "as opposed to just communicating through a consult letter." For about 5 percent of his patients, the retainer fee is waived.

Fugaro is partnered with another physician; neither leaves town unless the other can stay. Though always "on call," Fugaro said he has more time now for nonclinical professional pursuits. In 2007, he was elected president of the San Francisco Medical Society, where he pushes for such public health measures as restrictions on secondhand smoke, and partners with the California Medical Association to battle Medicaid cuts. He also has volunteered at a clinic in Mexico.

Fugaro says his colleagues' reactions have been mostly positive. Indeed, several are opening retainer-based practices of their own, including Treadwell, the physician who took over his old practice. Fugaro acknowledged that access to primary care is a tremendous problem in American medicine. "We need to create a better model for primary care doctors to continue doing what they're doing and be emotionally rewarded for it, as well as deriving reasonable economic compensation. And right now our system is broken in that regard." —Jenny Blair

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 or write to Faces, Yale Medicine, 300 George Street, Suite 773, New Haven, CT 06511.

NOTES



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Arthur Beaudet John Patti





Paul Rothman



Lu Anne Dinglasan Kevin Lau

Steven I. Rosenfeld, M.D. '80, is an assistant clinical professor of ophthalmology at the Bascom Palmer Eve Institute in Miami. He received two awards from the American Academy of Ophthalmology at its annual meeting in November 2007: the Senior Achievement Award and the Secretariat Award for "exceptional leadership and enthusiastic service." He serves on the editorial boards of EveNet Magazine, Focal Points, and the Basic and Clinical Science Course, Section 13: Refractive Surgery, and is an associate examiner for the American Board of Ophthalmology.

Paul Rothman, M.D. '84, was named dean of the University of Iowa's Roy J. and Lucille A. Carver College of Medicine, effective June 1. Rothman has served as head and professor of internal medicine at the UI Carver College of Medicine and UI Hospitals and Clinics since 2004. An expert in rheumatology, he has provided clinical care for more than 20 years, trained medical students, fellows, and residents, and published extensively. Rothman's research on cytokines focuses on their role in the development of white blood cells, the abnormal development of which can lead to leukemia.

2000s

Elizabeth K. Arleo, M.D. '04, and her husband, Joshua W. Thompson, J.D., announce the birth of their first child. Sophia Arleo Thompson was born on May 31 and weighed in at 8 lbs., 3 oz. Arleo is in the final year of a radiology residency at New York Presbyterian Hospital-Weill



Carolyn Graeber Robert Jahn

Cornell Medical Center, where she plans to stay for a year-long fellowship in women's imaging. Thompson is a partner at the New York City law office of Proskauer Rose.

Lu Anne V. Dinglasan, M.D. '08, and Kevin C. Lau, M.P.H., M.D. '08, were married on May 31 at the Yale Club in Manhattan. Dinglasan began an internship in June at Pennsylvania Hospital in Philadelphia and Lau began his internship at the Children's Hospital of Philadelphia.

Carolyn P. Graeber, M.D. '08, was married on April 26 to Robert E. Jahn at St. Thomas Episcopal Church in Manhattan. Graeber began an internship in June at the Memorial Sloan-Kettering Cancer Center in New York. Jahn is completing an M.B.A. at the University of Pennsylvania.

Mona Kotecha, M.D. 'o4, was married on April 5 to Nikhil Shanbhag, J.D. 'o3, in Saratoga, Calif. Kotecha is a fourth-year anesthesiology resident at the University of California, San Francisco. Shanbhag is an intellectual property lawyer at Google in Mountain View, Calif.

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Arthur L. Beaudet, M.D. '67, the Henry and Emma Meyer Professor and chair of the Department of Human and Molecular Genetics at Baylor College of Medicine, has been elected to the Johns Hopkins University Society of Scholars. Beaudet and 14 other esteemed scientists and clinicians were honored during the society's 39th induction ceremony in May. His accomplishments include key discoveries in several genetic disorders, including Angelman syndrome, Prader-Willi syndrome and autism. Beaudet's many honors include the March of Dimes/Colonel Harland Sanders Award for lifetime achievement in genetic sciences.

1970s

Harvey Berger, M.D. '77, and his wife, Chrysanthi, are ecstatic about the latest addition to their family, Isabella Grace Berger, born on March 6. Berger is the founder, chair and CEO of ARIAD Pharmaceuticals, Inc., in Cambridge, Mass., an oncology company developing molecularly targeted cancer drugs.

John A. Patti, M.D. '71, was elected vice chair of the American College of Radiology (ACR) Board of Chancellors at the ACR annual meeting in Washington, D.C., in May. Patti, a member of the radiology staff at the North Shore Medical Center in Salem, Mass., since 1975, is the immediate past chair of the ACR Commission on Economics, current chair of the Task Force on Value Added and vice chair of the Commission on Government Relations.

1980s

Josef Bohm, M.P.H. '89, will be joining the faculty of City University's New York City College of Technology as an assistant professor within their Health Services Administration program. Bohm is a former deputy principal to the Anglo-**European College of Chiropractic** in Bournemouth, England. He is a member of the adjunct faculty at the State University of New York at Stony Brook. His academic interests include behavioral economics, health policy and finance.

Jonathan S. Lewin, M.D. '85, has been inducted as a fellow in the American College of Radiology. Lewin is the Martin W. Donner Professor and chair of the Department of Radiology at the Johns Hopkins University School of Medicine. He holds leadership positions in such medical societies as the Academy of Radiology Research, Association of University Radiologists and the International Society for Strategic Studies in Radiology.

Troy Pappas, M.P.H. '86, has been appointed to the faculty of the Fox School of Business at Temple University in Philadelphia. He has a dual appointment with Temple's School of Tourism and Hospitality and will be teaching entrepreneurship and business strategy. This fall, he will teach entrepreneurism at Temple's College of Health Professions. He is the founder and president of World Athlete, a sports and fitness management company specializing in track and field. 62

Rex B. Conn Jr. M.D. '53, died of Parkinson disease on March 2 in Philadelphia. He was 8o. Born in Cedar Rapids, Iowa, Conn taught at West Virginia University in Morgantown, where he established the pathology department and clinical laboratory. He served as a radar specialist in the Navy Reserve during World War II. Conn was subsequently named to advisory committees at the National Institutes of Health, Walter Reed Army Medical Center and the Armed Forces Institute of Pathology. From 1968 to 1977 he taught at Johns Hopkins University School of Medicine. Conn ran clinical labs both there and at Emory University, where he also taught. In 1987 he moved to Philadelphia, where he taught at Thomas Jefferson Medical College until his retirement in 2003.

Alfred Robert Cordell, M.D., H.S. '50, died on April 9 in Winston-Salem, N.C. He was 83. After receiving his medical degree and completing an internship at Johns Hopkins University, Cordell came to the Yale VA Surgical Services for an assistant residency in surgery from 1948 to 1950. Following a stint as a surgeon with the Medical Corps, U.S. Navy Reserve, training in general and thoracic surgery at Wake Forest University, and a year as a visiting instructor in the Department of Surgery at the University of Buffalo, he returned in 1970 to Wake Forest. where he became a professor of surgery. From 1979 to 1991 he served as the Howard Holt Bradshaw Professor of Surgery and chair of Wake Forest's Department of Cardiothoracic Surgery. Cordell developed

techniques in myocardial preservation and blood conservation and established an open-heart program at Wake Forest's Baptist Medical Center. He served on the board of governors of the American College of Surgeons from 1983 to 1989. In September 1995, he was named professor emeritus at Wake Forest; the A. Robert Cordell Chair in Cardiothoracic Surgery was established in his honor.

Roger W. Davis Jr., M.D. '43, died on March 16 in Springfield, Vt. He was 90. After graduation from medical school, Davis completed internships at Hartford Hospital in 1943 and 1946. From 1944 to 1946 he served with the U.S. Army's 174th Engineer Combat Battalion. He completed residencies in orthopaedic surgery at the Hospital for Special Surgery in New York City from 1947 to 1949 and at Boston City Hospital in 1950. He opened a private practice in orthopaedic surgery in Hartford and worked as assistant medical director of the Aetna Life and Casualty Co. From 1974 until his retirement in 1981, he served as a part-time physician in Springfield Hospital's emergency room.

D. Joseph Demis, PH.D., M.D. '57, died on March 8 in Clifton Park, N.Y. He was 78. After interning in Seattle, Demis took a fellowship in biochemistry at Oxford University. There he explained the biosynthetic pathway of adrenaline in mammalian tissue and performed pioneering studies that showed the effectiveness of antimetabolites as treatment for psoriasis and similar skin conditions. He received further training in dermatology at Walter Reed Army Hospital in

Washington, D.C. His interest in tropical diseases, and especially pinta, a bacterial skin disease endemic to Central and South America, led him to the U.S. Public Health Service. Working with the Brazilian government, Demis helped to eliminate pinta in that country. Demis subsequently served as professor and chair of dermatology at Washington University in St. Louis from 1964 to 1966; at that time he was the youngest chair of a major dermatology department in the United States. After accepting an appointment as professor and chair of dermatology at Albany Medical College, he collaborated to produce the text Clinical Dermatology. He also maintained a private dermatology practice.

Frederick James Finseth, M.D., died in February in San Francisco. He was 67. A graduate of Harvard Medical School, Finseth completed a residency in surgery at Massachusetts General Hospital. He was assistant professor in reconstructive and plastic surgery at the School of Medicine from 1974 to 1977. He published several papers on the impairment of blood flow in the hand from cigarette smoking during his years at Yale. From 1977 to 1979 Finseth was an assistant professor in plastic and reconstructive surgery at Stanford University School of Medicine, specializing in reconstructive surgery of the hand. He traveled widely and made annual trips to teach at Tata Memorial Hospital in Mumbai, India. He also taught in South America, Singapore, China and South Asia.

Steven C. Hebert, M.D., chair and C.N.H. Long Professor of Cellular

and Molecular Physiology and professor of medicine, died of cardiovascular disease in New Haven on April 15. He was 61.

Hebert was a board-certified nephrologist who devoted his career to the science of renal fluid and electrolyte regulation. He made major contributions to medicine, notably in the cloning of genes that mediate or regulate the transport of sodium, potassium and calcium across cell membranes. His work won him election to the National Academy of Sciences in 2005, and his research was the basis for a new class of drugs used to treat hyperparathyroidism, a hormonal disorder that affects many of the more than 1 million patients worldwide with endstage kidney disease.

Hebert was born in 1946 in Rockford, Ill., and lived for part of his childhood on the island of Great Inagua in the Bahamas, where his father was a contractor for the Morton Salt Co. In a profile published in 2006 in the Proceedings of the National Academies of Sciences, he recalled watching bulldozers pile dried sea salt into mountains 150 feet high and speculated that his interest in metabolic salts may have had its genesis there. He entered Florida State University at age 15 and graduated after three years.

Hebert received his medical degree from the University of Florida in 1970. Following training in internal medicine and nephrology at the University of Alabama at Birmingham (UAB), he served on the faculty at UAB, Eastern Virginia Medical School, the University of Texas Medical School in Houston, Harvard Medical School, and Brigham and Women's Hospital. In 1997



he joined Vanderbilt University as director of the Division of Nephrology and the Ann and Roscoe R. Robinson Professor of Medicine. In 2000 he was offered the chair at Yale, which gave him the opportunity to lead a world-class department and continue his close collaboration with Gerhard Giebisch, M.D., a longtime friend and mentor.

In the early 1990s, Hebert's laboratory made three fundamental discoveries about the kidney's processing of potassium, sodium and calcium. His group identified a channel that regulates potassium excretion and is involved in Bartter syndrome type II, an inherited disorder that causes loss of sodium and potassium through the urine. He and his colleagues also identified two sodium chloride transporters that are target sites for important diuretic drugs. His subsequent discovery of a calcium-sensing receptor known as CASR led to the development of a new class of drugs that modulate calciumreceptor activity.

Most recently, with John Geibel, M.D., D.SC., Hebert demonstrated in an animal model that diarrhea could be reversed almost immediately by activating the CASR receptor. Such treatment would have a major impact on health problems in developing countries, where diarrheal disease kills some 3 million infants and children each year.

Hebert was awarded numerous professional honors, including the Homer W. Smith Award from the American Society of Nephrology, the A.N. Richards Award from the International Society of Nephrology, and the Carl W. Gottschalk Distinguished Lectureship from the American Society of Physiology. Virginia H. Hulbert, R.N., M.P.H. '50, died on January 31 in Ansonia, Conn. She was 97. After earning her degree in nursing, Hulbert worked for more than 30 years as an assistant professor of health at Southern Connecticut State University, and as head nurse in the school's student health department.

D. Frank Johnson Jr., M.D. '55, died on March 31. He was 78. After completing his internship, Johnson joined the Air Force as a flight surgeon. Following a residency in internal medicine at Minneapolis General Hospital, in 1961 he pursued a career in Billings, Mont. For 25 years he was the continuing medical education director for St. Vincent Hospital, where he founded and directed Montana's first cardiac rehabilitation program. He also helped to develop St. Vincent's ICU, its weight control program and its Lifecare outpatient clinic. He was an associate clinical professor of medicine at the University of Washington School of Medicine in Seattle. Later in his career he focused on weight management, directing clinics in Billings, Helena and Bozeman, Mont., while continuing to serve airline pilots in the state as a senior aeromedical examiner designated by the Federal Aviation Administration. He was a member of the North American Society for the Study of Obesity. Among other honors, Johnson received the American Society of Bariatric Physicians' Bariatrician of the Year award in 2002.

Vincent J. Longo, M.D. '46, died on February 18 in Niantic, Conn. He was 85. During World War II, Longo was a member of the Army Specialized Training Program and received a commission as first lieutenant. Following an internship in surgery, gynecology and obstetrics, and a fellowship in urology, he began a urology practice in New London, Conn., in 1952. He joined the staff of Lawrence and Memorial Hospital in New London and served as chief of urology there from 1976 until his retirement in 1986. Longo was a member of the American Board of Urology, a fellow of the American College of Surgeons, and a certified sex educator and therapist with the American Association of Sex Educators, Counselors and Therapists. After retiring he served with Charles Pfizer Pharmaceuticals as principal clinical investigator in the Viagra program.

Gordon V.K. Reid, M.D., H.S. '69, died on April 15. He was 72. After receiving his medical degree from the University of Rochester and further training at Barnes Hospital in St. Louis, Reid served as U.S. Public Health Service lieutenant commander in the Epidemic Intelligence Service of the Centers for Disease Control and was sent to India to do smallpox eradication. In 1968 he came to Yale to finish his training in internal medicine, endocrinology and gerontology. Shortly after joining a New Haven practice in 1970, he co-founded the Community Health Care Plan, where he practiced until 1999. He then co-founded Endocrine Associates of Connecticut, Reid was an associate clinical professor of medicine at Yale, attending in internal medicine and endocrinology, and a preceptor for residents from Yale-New Haven Hospital and the Hospital of Saint Raphael.

Galon S. Rodabaugh, M.D., H.S. '53, died on January 9. He was 95. Rodabaugh completed his medical degree and internship at Ohio State University in 1939; practiced for several years in Basil, Ohio; and served from 1942 to 1945 as a captain with the U.S. Army Medical Corps in England, France, Belgium, Holland, Luxemburg and Germany. He saw combat during in the Battle of the Bulge and received two Bronze Stars. After completing a residency at Yale in 1953, he served as anesthesiologist at the Fairfield Medical Center in Lancaster, Ohio, until his retirement in 1984.

William G. Wysor Jr., M.D., H.S. '52, died on January 3 in Chapel Hill, N.C. He was 81. After receiving his medical degree from the University of Virginia, Wysor received post-graduate training at Yale and the Medical College of Virginia. In 1953 he entered private practice in South Boston, Va. From 1957 to 1969 he served as associate professor of medicine at the University of North Carolina (UNC) School of Medicine. From 1969 until his retirement in 1990, he practiced with Durham Internal Medical Associates. His honors included teaching awards from Escola Paulista de Medicina in São Paulo, Brazil, where he was a visiting professor, and from the UNC School of Medicine.

SEND OBITUARY NOTICES TO Claire M. Bessinger, Yale Medicine, 300 George Street, Suite 773, New Haven, CT 06511, or via e-mail to claire.bessinger@yale.edu

Follow-up

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After a life in medicine, a career in show business

Brock Lynch, M.D. '47, had been singing and dancing with the Young@Heart Chorus for almost 10 years when it was written up in *Time* magazine in June of 2005, and in *Yale Medicine* [See "Tap Dancing Through Medicine," Autumn 2005]. Since the documentary *Young@Heart* was released in April, Lynch and the other performers in the 27-member Massachusettsbased group of elderly rock singers continue to tour to even greater acclaim.

"Little by little, instead of drooping, it grew," Lynch said of the film, which was released only gradually in the United States. Word of mouth and a free showing at the Sundance Film Festival soon accelerated the film's popularity, and chorus members have subsequently traveled not only to perform but to promote the film. Just prior to its release, Lynch traveled to Washington, D.C., and Boston with two other chorus members to answer questions from an audience of critics.

Children, adolescents, and college-aged audiences, he has long noticed, enjoy the live shows the most, while the older demographic seems less appreciative. "They don't go for that music—that was the music [about which] they told their children, 'Turn it down!' " But now that many audience members have seen the film, Lynch said, the group has "rabid devotees."

Lynch recently sang with Young@Heart in Manhattan at the historic Beacon Theater on Broadway, a mile from Memorial Sloan-Kettering Cancer Center, where he was a surgical teaching fellow in the mid-1950s. The "Alive and Well" concert tour also included stops in Boston and the group's home base of Northampton, Mass. The set list included songs by the Rolling Stones, Nirvana and James Brown.

The group plans next to develop a cabaret act, heavy on the soloists. More tours are also in the works. How do they do it? "With grit, guts and good medication," said Lynch.

—Jenny Blair

Archives 50 AND 25 YEARS AGO



Report on Alumni Day —Alumni Bulletin May 1958

"In spite of a heavy snowfall the preceding weekend and snow flurries on the morning of Saturday, February 22, many Yale Alumni in Medicine turned out for the annual Alumni Day activities at the school. Almost 200 were present at the afternoon business meeting in Fitkin Amphitheater. Dr. Samuel D. Kushlan ('35) presided, Dean Vernon W. Lippard spoke briefly on recent developments at the medical school. Those attending then heard a lively discussion of coronary heart disease by Dr. Jeremy N. Morris, visiting professor of epidemiology."



The Case of Three Missing Hamsters —Yale Medicine Fall / Winter 1983

"Three infected hamsters reported missing from their cage in the animal containment facility on the ninth floor of the Laboratory of Epidemiology and Public Health became overnight celebrities of a sort. 'Infected Yale Hamsters Escape' was headline news for the wire services, major television and radio networks and newspapers across the nation, including the *New York Times*, which devoted almost half a page to the story.

"The hamsters have not been found, and are presumed dead. Although their disappearance caused considerable stir in the media and concern in the University, the three rodents and others like them in the LEPH-9 facility are of little threat to human health and the likelihood that they escaped from the facility is practically nil....

"The hamsters were among several hundred research animals in a major study of Alzheimer's disease ... [they were] infected with Creutzfeld-Jakob virus, a socalled 'slow virus,' which is invariably fatal, and causes symptoms of senility similar to those of Alzheimer's disease. ...

"A series of meetings has since been held to ascertain facts of the escape, and to plan remedial actions."

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PRETTY IN PINK

During the academic year, the stainless steel tables in The Anlyan Center's anatomy labs hold the "donors" who have offered their bodies for the education of future doctors and physician associates. For most medical students this introduction to medicine is a charged and emotional experience. In May the students who completed this first-year course spent two days wrapping pink fabric around the tables where they'd dissected the human body. Their inspirations were the artists Christo and Jeanne-Claude, known for their wrappings of such public spaces as the Pont Neuf in Paris.

"To mark the school year's end, student artists have this time wrapped the lab itself, transforming this familiar space and raising critical questions about our relationship to anatomy," wrote Ryan Blum in the program for the installation, called Recovering the Anatomy Lab. The installation was open to visitors for about two weeks in May and June. "What is hidden in the site of dissection? What damage have we done, and how can we make amends? Can and should the lab be made beautiful? What about ourselves is changed? How can we help future classes of anatomy students with this difficult practice?"

About 50 students gathered to bind the anatomy tables in bolts of fuchsia cloth, said Michael Otremba, who conceived of the idea with classmate Lauren Graber. "It's a sterile, metallic environment," said Otremba, adding that students wanted to comment on what he called "an emotionally significant time." The choice of pink was deliberate. "We wanted to be playful."

"I think it's delightful," said William B. Stewart, PH.D., associate professor of surgery (gross anatomy), who has been guiding Yale medical students through the human body for 30 years. "Art is all about people coming to grips with their feelings."

-John Curtis



Evoking the work of artists Christo and Jeanne-Claude, students wrapped dissection tables in the anatomy lab in pink cloth, an installation that helped them deal with their own reactions to the first-year course.

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ON THE COVER

The Smilow Cancer Hospital and related structures are changing the face of the medical center neighborhood. Õ

CAMPUTARO

THIS PAGE

Construction projects at the medical center are bringing safety and traffic improvements to the neighborhood.

Photographs by Robert Lisak

WINTER 24



GROVE

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As the medical center grows, so grows the city The ongoing expansion of the medical center fits in with New Haven's own plans to undo past urban renewal mistakes. By Jenny Blair

Science and culture in a strange land

As the world gets smaller, the Committee on International Health asks whether Downs fellows need to leave home to find a foreign experience. By John Dillon

The lost art of the physical exam

Physicians once relied on seeing, hearing and touching a patient to make a diagnosis. Technology has enhanced those skills, but many doctors lament their decline. By Jill Max

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President and dean respond to economic downturn

Although the university and the medical school remain strong financially, the economic downturn requires some adjustments, both President Richard C. Levin and Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, cautioned recently in separate messages to faculty and staff.

The economic situation, described as the worst since the Great Depression, had reduced Yale's endowment by \$6 billion, "a decline of 25 percent since June 30, 2008," Levin announced in December. Budget shortfalls of about \$100 million are expected next year and more than \$300 million by 2013-14. Nevertheless, Levin said, "\$17 billion is still a very large endowment."

"In spite of the challenges before us, we shouldn't forget that we entered this period on a very strong footing and we remain strong," Alpern wrote on January 23. The school has seen consistent growth in NIH funding over the past few years, as well as growth of 11 percent in clinical collections during the first half of the current fiscal year. Gifts and pledges have also been rising in recent years.

The university and the medical school, however, must tighten their belts.

Levin said that next year's budgets will be reduced by an

amount equal to 5 percent of the salaries and benefits of all nonfaculty and staff, largely through attrition. Budgets for all nonsalary and wage expenses will be reduced by 5 percent next year and by an additional 5 percent the following year. Employees in labor unions will receive the increases scheduled for the final year of their contracts, and nonunion employees will be eligible for merit increases of up to 2 percent, up to a cap of \$1,500. He urged staff and faculty to save money by spending less on outside consultants, reducing travel, consuming less paper and decreasing energy use. New building and renovation projects under construction will continue, but most new construction will be deferred, although design work will continue.

The medical school will follow these guidelines, Alpern said, while noting that its financial picture is somewhat different. The university budget draws 44 percent of its income from the endowment, but endowment income accounts for only 8 percent of the medical school's \$988.6 million budget, which comes largely from research grants and clinical income. The central administration budget, however, draws 17 percent of its revenues from endowment income. Tuition and philanthropy together account for 5 percent of the medical school's income.

Alpern vowed to try to "protect our employees in these uncertain economic times," while honoring commitments made in recent years.

"We will maintain our commitment to expanded financial aid," he said, referring to a new financial aid policy that eliminates parental contributions from families making less than \$100,000 per year. Recruitment of faculty and staff will continue, but hiring decisions will be considered carefully by the dean's office and the provost's office. Development of programs for West Campus will also continue.

"This is no time to back off from our core values and goals, and by making well-considered, strategic decisions now, we stand to do well in the future," Alpern said. "We will continue to be a school that seeks new knowledge in the service of humanity, finds new ways of diagnosing and treating illness, and produces new leaders in science and medicine. To reach these goals, I ask all of you to help."

CORRECTION: REUNION REPORTS Alvin B. Blaustein, M.D. '48, and

Alvin B. Blaustein, M.D. '48, and B. Herold Griffith, M.D. '48, wish to correct references to themselves in the reunion report of the Class of 1948, published in the Autumn 2008 issue of *Yale Medicine*. Blaustein noted that there is more than one member of the class still in practice: he remains active in psychoanalytic practice in New York City. Griffith said that he was a professor of surgery and chief of plastic surgery at Northwestern University, not at the University of Illinois.

starting Point

vale medicine

Alumni Bulletin of the Yole University School of Medicine Winter 2009, Volume 43, No. 2

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Yole Medicine is distributed to alumni, faculty, students and friends of the School of Medicine, as well as to leaders in Yale University alumni activities.

Abbreviations commonly used in Yale Medicine include HS to denote the final year of residency for house staff, FW for the final year of a fellowship, EPH for the Department of Epidemiology and Public Health and the School of Public Health and YNHH for Yale-New Haven Hospital.

Postal permit held by Yale University, 155 Whitney Ave., New Haven, CT 06520

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Two faculty members move on, but remain close at hand

Eleven years ago when I started as a staff writer here at *Yale Medicine*, one of the first people I met was Michael Kashgarian, M.D. '58, Hs '63, whose name appears on our masthead as editor in chief. Since then, over lunches at Mory's, meetings in conference rooms and chats in our offices, we've discussed the direction of the magazine in both generalities and specifics. He's suggested story ideas and people to talk to, as well. What Mike Kashgarian always brings to these conversations is a love of both Yale and *Yale Medicine*. He sees the two as linked, with the magazine providing a way to keep alumni involved with the institution. Mike officially retired as of last July I, but he's staying on as a researcher until he finishes a few remaining projects, and he remains editor in chief of *Yale Medicine*.

In those days another member of the faculty I came to know was Asghar Rastegar, M.D. Although he plays no direct role in *Yale Medicine*, time and again we turned to him as a source for stories about an eclectic range of topics—collaborations with medical schools in Russia and Uganda, a Yale delegation in Iran, the challenges of implementing the 80-hour work week for residents and, for this issue, the declining art of the physical examination. It wasn't just because of his role as deputy chair of internal medicine or his prominence in setting the direction of medical education at Yale. Nor was it his knowledge of medicine or of Yale that kept leading us to him. His knowledge goes beyond expertise and rises to the plateau of wisdom, which he has shared with us with grace and generosity. Even though he has stepped down from his administrative post in internal medicine, he'll stay on as director of the international health program that sends residents abroad for rotations in underserved settings. As with Mike Kashgarian, it's reassuring to know that Asghar Rastegar will still be close at hand.

John Curtis Managing Editor

SECOND OPINION BY SIDNEY HARRIS



"OH, OH - THE VACCINES!"

3

Reform of premed education under way

Medical educators are taking a fresh look at undergraduate courses that may deter students from medicine.

In 1910, Abraham Flexner's examination of the state of American medical education led to widespread reforms in the way doctors are trained. Today, another evaluation is under way that could have equally far-reaching ramifications for future physicians.

The Committee to Establish the Scientific Foundation for Future Physicians, organized by the Association of American Medical Colleges and the Howard Hughes Medical Institute, is studying the standard premedical curriculum to make it more relevant to the practice of modern medicine.

Robert J. Alpern, M.D., dean and Ensign Professor of Medicine, the committee's co-chair, said it took the committee only a single meeting to identify the problem: while science and medicine have changed dramatically since the days of Flexner, the premed curriculum has remained static. Organic chemistry, the bête noire of almost every premed student, is a required course although the relevance of some components of the course to medicine is marginal. At the same time, such crucial subjects as statistics, biochemistry and genetics aren't required at the undergraduate level.

Another problem, Alpern said, is that the premed curriculum often serves as a gatekeeper to weed out students. "I've actually spoken to organic chemistry professors who pride themselves on being the ones who determine who should go into medicine," he said.

The 19-member committee, drawn from both medical schools and undergraduate institutions, has been meeting for about a year and a half. It's working on recommendations that will be presented in a report this year.

The key proposal, Alpern said, is to replace required courses with "scientific competencies"—the knowledge and habits of thought that a student should have upon entering medical school. "We want to get away from telling colleges, 'You need to have a course in this or a course in that,' " he said. "We want to say, 'These are the competencies someone should have.' "

Alpern anticipates that this approach will reduce the importance of organic chemistry in favor of biochemistry. Similarly, the mathematics curriculum will shift away from calculus and toward statistics. Alpern also hopes that professors will develop interdisciplinary courses that illuminate the medical relevance of premed coursework and that standardizing what new medical students should know will free medical school professors from having to teach to the lowest common denominator.



Dean of Yale College becomes third scientist named as provost

Last fall, during his final freshman address as dean of Yale College, Peter Salovey, PH.D. '83, exhorted members of the Class of 2012 to go their own way, to "say goodbye to what is familiar, even to what we have grown to love, and leave it for uncharted waters."

He could have been giving himself a pep talk in the bathroom mirror. After four years as dean, a job he readily admits he loved, Salovey was offered the job of provost, the university's chief academic officer after the president. "I'm delighted to have this new set of challenges," he said, "but to walk away from something you love is a difficult thing to do."

Salovey, the Chris Argyris Professor of Psychology and professor of epidemiology and public health, is Yale's third consecutive provost to be chosen from the health-related sciences. He succeeds Andrew Hamilton, PH.D., an organic chemist who left Yale to become vice chancellor of the University of Oxford in England, and Susan Hockfield, PH.D., a neurobiologist who is now president of the Massachusetts Institute of Technology.

Salovey doesn't think this is a coincidence. "There is no doubt that for Yale to remain in the top tier of universities, we have to strengthen science and engineering on both sides of campus," he said. "This is an area of priority and has been for some years."

The acquisition of West Campus, a former pharmaceutical company lab and office complex in neighboring West Haven and Orange, is critical to this effort, Salovey said, and he sees it as part of his new job to work with Michael Donoghue, PH.D., the vice president for West Campus Planning and Program Development, to use that facility as an incentive to attract worldclass researchers to Yale.

Noting his numerous research collaborations with faculty from the schools of medicine and public health (he was co-director of the Center for Interdisciplinary Research on AIDS for nine years), Salovey said he understands the challenges faced by the medical school faculty. "My lab has the same pressures," he said. "We look for funding the same way. We share the same struggles." 5

Salovey joined the Yale faculty in 1086 after receiving his undergraduate degree from Stanford and his PH.D. from Yale. He was appointed dean of the Graduate School of Arts and Sciences in 2003. A year later, he was named dean of Yale College, where he presided over growth in international programs and financial aid changes. His research has focused on human emotion and health psychology. With colleague John D. Mayer, PH.D., he developed a concept called "emotional intelligence," the theory that just as people have a range of intellectual abilities, they also have measurable emotional skills that affect their success in life.

Salovey knows his own emotional intelligence will be tested in his new job. "The stereotype of the provost's office is the guy who says no," he said. "But I think it's a mistake to assume that the role of the provost is to frustrate all good ideas, intentions and creativity of the faculty. I would like to think of it as the office that helps you shape your ideas, clarify your goals and manage your expectations so that we can be saying 'yes' at least as often as we say no."

-J.K.



Peter Salovey

The impetus for revisiting the premed curriculum came from the National Research Council's 2003 BIO 2010 report, which found that fewer American students are becoming research biologists—in part because of the premed requirements. "When premed students got tortured in organic chemistry, people thinking about careers in research biology got tortured along with them," Alpern said.

Committee members plan to seek feedback from certain medical and undergraduate educators before disseminating the report to the undergraduate and medical school communities. The committee knows it will be easier for wealthy colleges to revise their curriculum to accommodate these changes.

In a parallel effort, a new committee has been formed to revise the MCAT, the aptitude test that students take for admission to medical school. The work of these two committees must be integrated for change to occur as it requires coordinated modifications in premed requirements, the MCAT and the undergraduate curriculum. Alpern predicts it will take some years before students see any changes, because directors of undergraduate programs will need to know how the MCAT will be revised before they can change their curricula.

"It's not going to happen overnight," he said, "but when it does, I think it will represent a major transformation in medical education." —Jennifer Kaylin

Online: Yale Netcasts

Online: Yale Netcasts Robert J. Alpern: Vision for the School of Medicine

A physician's gift supports research on pre-eclampsia and prematurity

Shortly before the end of World War II, a dying Albert S. McKern, м.А. '13, M.D., turned to lawyers—fellow prisoners in a Japanese internment camp in Sumatra-and composed his will. His vacant land was to be developed, and property that he owned in Penang, Malaysia, where he had practiced as a physician and surgeon, was to be renovated and rented. Ten years after the death of his last child, the family's holdings were to be sold and the money divided among three universities-Yale, where he had received a degree in engineering; the University of Sydney in Australia, where he had received his bachelor's degree and studied theology;

and the University of Edinburgh in Scotland, where he had received his medical degree.

Born in 1885 in Sydney, McKern came to Yale in September 1911 after deciding that theology was not for him because of his difficulties with public speaking. He earned a master's degree from Yale, followed by a medical degree from Edinburgh in 1917. McKern then moved to Penang, where he built up both a successful medical practice and substantial real estate holdings. During the Japanese invasion in 1942, McKern was captured in Indonesia. He died three years later of dysentery.

Under the terms of McKern's will, his family's estate—\$12 million—was to be used "for the sole and special purpose of establishing medical research scholarships for investigation into the

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Albert McKern in Penang, Malaysia, circa 1937. In 1947, statesman Averell Harriman of the Yale College Class of 1913 sought McKern's help on behalf of the Yale-in-China Association, only to learn of McKern's death. causes, prevention and treatment of mental and physical pain and distress during pregnancy, labour and the puerperium." McKern's last surviving beneficiary died in December 1997, and the trust terminated a decade later.

Yale's portion of McKern's giftabout \$4 million—will endow annual grants to those doing promising research on these issues. Charles I. Lockwood, м.р., the Anita O'Keefe Young Professor of Women's Health and chair of obstetrics, gynecology and reproductive sciences, learned about the gift several years ago at a meeting with Andrew A. Calder, м.D., head of reproductive and developmental sciences at Edinburgh. Lockwood's initial reaction was disbelief. "He'd had a few drinks and I thought he was exaggerating," Lockwood said. Eventually the two began a discussion of joint work that might fulfill McKern's dream.

"They have a very strong program," he said of ob/gyn research at Edinburgh, citing the work done in prematurity and pre-eclampsia in particular.

Lockwood hopes to devise a joint strategy for using the money from the bequest during this academic year. Given McKern's desire and the needs of the field, Lockwood sees prematurity research as an area of focus. "[Prematurity] is the leading cause of infant mortality in the United States, the leading cause of mental retardation, the leading cause of childhood blindness. It costs the U.S. economy around \$28 billion a year in terms of health care-related resources. Preterm delivery is a national public health crisis."

Funds from the bequest may also support a Yale-Sydney-Edinburgh scholarly exchange program and research on postpartum depression in the psychiatry department.

-Charles Gershman



UNIVERSITY MANUSCRIPTS AND ARCHIVES

VALE

Online: Yale Netcasts Charles J. Lockwood : Yale Ob/Gyn—Research Updates and Clinical Advances

Yale team builds new search engine that retrieves images based on embedded text

In July a team of Yale scientists published a paper describing an innovative search engine with a new way of finding biomedical images. Search engines and websites already allow scientists to search for images based on titles and captions. "We are not aware of a biomedical search engine that can retrieve images by searching the text within biomedical images," Michael O. Krauthammer, M.D., PH.D., assistant professor of pathology, and colleagues wrote in their paper published in *Bioinformatics*.

The Yale Image Finder (YIF) lets researchers locate diagrams, graphs and other experimental figures based on text contained in the images. YIF, funded by a grant from the National Library of Medicine and accessible at http://krauthammerlab.med.yale.edu/ imagefinder/, enables users to access more than 140,000 images from more than 34,000 papers published in openaccess biomedical journals.

Krauthammer calls this new technology a major step in biomedical literature retrieval, as most important information exists in places other than image captions, which, until now, have been the primary targets of image search engines.

YIF functions by performing optical character recognition before making the images available for search. Users can restrict image queries to the text within the images, the image caption, the paper title, paper abstract, full text or any combination thereof. After submitting a query, YIF presents users with



Yale scientists have devised a way to search biomedical images based on text contained in the images.

thumbnails of images. Once an image of interest is selected, YIF provides a high-resolution version of the image, along with the abstract, full text and other images from the associated paper.

"The idea is to augment text mining with image mining, with the idea that we can have a better understanding of a research article using automated means," Krauthammer says. "I've felt that images are undervalued in terms of their representative quality and what type of information they can hold. In the future, we should be able to obtain even more information from the images, and get a pretty good understanding of what the paper is about."

-C.G.

et cetera ...

TWO GRANTS ADVANCE PUBLIC HEALTH

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The School of Public Health has received a twofold boost in the form of an \$11 million grant from the National Institute of Mental Health (NIMH) and a \$10.7 million grant from the National Institute of Child Health and Human Development (NICHD).

The NIMH funding provides five years of support for HIV/AIDS prevention and health services at the school's Center for Interdisciplinary Research on AIDS (CIRA). The grant from NICHD adds to a \$15 million grant in 2007 to support Yale's role in a national study that will follow 100,000 children from before birth to age 21 to improve understanding of the factors that contribute to their health and development.

The grant to CIRA follows an October 2008 report from the Centers for Disease Control and Prevention that revealed higher estimates of new HIV infections in the United States than previously calculated and emphasized the need for more rigorous study of interventions for HIV prevention.

—John Curtis

YALE PAYS \$7.6 MILLION IN GRANTS PROBE

Under the terms of a settlement reached in December, Yale will repay the federal government \$7.6 million after an investigation of Yale's accounting practices for research grants. The probe, which began in June 2006 and covered periods going back to 1999, was led by the U.S. Attorney's Office on behalf of federal granting agencies, including the Department of Health and Human Services and the National Science Foundation.

President Richard C. Levin said that the university has "a clear obligation to comply with all regulations pertaining to the administration of federal awards." He also acknowledged that federal regulations are sometimes burdensome, but noted that Yale receives more than \$400 million in federal grants each year.

As a result of the investigation, Yale's Office of Research Administration has developed training and education programs, published revised policies and procedures, implemented a Web-based reporting system, and designed procedures for the documentation and review of cost transfers.

—Ј.С.



Blood test in the OR speeds surgery

Measuring hormone levels in hyperparathyroidism on the spot sends patients home faster.

Since Robert Udelsman, M.D., M.B.A., department chair and the William H. Carmalt Professor of Surgery, came to Yale in 2001 to lead the medical school's Department of Surgery, the number of parathyroid operations has risen from about 30 a year to more than 350.

Most of these patients have primary hyperparathyroidism (HPTH)—one or more of the parathyroid glands in the neck begins to enlarge and produce too much hormone. These enlarged glands are called adenomas, and too much parathyroid hormone, or PTH, causes osteoporosis, kidney stones and other health problems. The adenoma needs to be removed, a procedure that usually requires general anesthesia and a stay of several days in the hospital.

Udelsman, however, has combined existing techniques with a simple but radical innovation—placing a laboratory machine to measure hormone levels inside the operating room—to turn this into an outpatient procedure.

"Patients can fly in on Sunday, get a place at the hotel and see us on Monday morning. Tuesday morning they come have surgery," said Patricia Donovan, R.N., M.B.A., Udelsman's clinical coordinator. "They return Friday that same week. They might explore New Haven, have their sutures removed ... and fly back."

Udelsman's approach, which has been adopted by the other three endocrine surgeons on the team, involves several steps. First comes pre-op preparation. In addition to the patient's medical history, the team needs to know where the offending adenoma is located. Most people have four or more parathyroid glands, so figuring out which is the overactive one —or whether there is more than one can be a challenge. Imaging studies help to localize it. Before the patients arrive for surgery, Donovan gathers relevant records, medical information and scan results, talking by phone with patients and their doctors to make sure that the surgery is appropriate for them.

In the operating room the uniqueness of Yale's approach becomes evident. Instead of patients being placed under general anesthesia, patients receive a series of injections of local anesthetic in the neck. A small incision is made, the offending adenoma is removed and a blood test is done to check levels of PTH. But rather than sending the blood sample to a laboratory, the technician in the operating room tests hormone levels immediately. The surgical team waits only 12 minutes for the results-about a guarter of the time needed at other institutions, where waiting for results can take longer than the operation itself. If PTH levels have dropped sufficiently, the surgeons can be confident that they removed the adenoma completely. Then it's time to sew up.

The entire procedure typically takes half an hour, and the patient goes home —or to the hotel—a few hours later, returning to the clinic in three days for a final follow-up visit. Complication rates are low, cure rates are about 98 percent and the surgery is cost-effective. But most of all, patients are satisfied.

—Jenny Blair

As doctors hand off patients, miscommunication at sign-outs can cause errors

"Sign-out," the conversation at shift change when hospital patients' information is handed off from one team of doctors to another, is the delicate hinge on which much medical communication turns. But this commonplace event can be fraught with miscommunications that frustrate doctors and pose a hazard to patients.

That's because doctors don't have a standard approach for sign-out—unlike those for the formal history and physical presentation—nor are they supervised when first doing it. "We have no training at all; there's nothing," said Leora I. Horwitz, M.D., assistant professor of medicine. Instead, residents wing it: they might painstakingly explain the team's reasoning for each patient's plan of care—or they might simply read names and diagnoses to a colleague and append a few comments to the list.

Because much of what is known about sign-out is anecdotal, Horwitz decided to study the practice. She and her team studied eight teams' hand-offs over 12 days, audiotaping evening sign-outs and collecting doctors' printouts, then asking the covering team in the morning if there had been any sign-out-related problems overnight.

There certainly had been. In 88 signout sessions, 24 sign-out-related problems came up. Fifteen related to inefficient care—the covering team had to duplicate work or research—but there were five episodes of delayed diagnosis or care and four close calls. In one case of miscommunication, a patient was transferred to intensive care in part because the covering team had not been warned about her bronchospasm.

These results, published in the September 8 *Archives of Internal Medicine*, will surprise few physicians who have had to start from scratch while caring for a colleague's patients. But with reductions in residents' work hours, a rising hospital census and a national impetus to reduce medical errors, sloppiness at sign-out is evolving from nuisance to pressing concern.

How should clinicians sign out? They might start by looking outside medicine. Other groups involved in high-risk or error-prone work, including the nuclear power, automotive and airline industries, have developed effective methods of handoff. "They teach it, they train it, they concentrate on it—which we don't do," Horwitz said. "What you want to hand off in person or on paper is the higher-order stuff, the clinical reasoning part, the synthesis, the judgment. Handoff is about understanding."

Based on these results, the internal medicine department began a sign-out curriculum for residents that is now in its third year. Horwitz often teaches it, and she has also developed sign-out templates for hospital residents in other specialties. She plans next to study signout during hospital discharge.

"We just haven't thought about [sign-out] as part of our job," she said. "We don't prioritize this as a safety issue, and that's part of what [our team is] trying to change by pointing out what goes wrong."

—Ј.В.

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NEW APPROACH TO THYROID SURGERY

Over the last two years the Yale Pediatric Thyroid Center has treated 30 patients by using a new approach—the pairing of pediatric and adult surgeons in the operating room. The center may be the only facility in the United States exclusively devoted to the care of children with thyroid conditions.

"The right surgical expertise is important for optimizing outcomes, because the area by the neck is delicate, especially in young children," said Scott Rivkees, M.D., professor of pediatrics and director of the center.

Since far more thyroid surgeries are performed on adults than on children, Yale physicians combined the expertise of Robert Udelsman, M.D., M.B.A., department chair and the William A. Carmalt Professor of Surgery, a high-volume adult endocrine surgeon, with the skills of Christopher Breuer, M.D., a pediatric surgeon versed in the challenges of treating thyroid disorders in young patients.

"We can tell parents, 'You're going to have one of the world's most experienced endocrine surgery teams working on your child,' " Udelsman said.

—Jennifer Kaylin

PREVENTING FALLS IN ELDERLY PATIENTS

Teaching clinicians and older patients how to prevent falls can reduce the likelihood—by up to 11 percent—of falls that lead to hospitalization or an emergency room visit, Yale researchers reported in *The New England Journal* of *Medicine* in July.

The researchers compared injury rates in a 58-zip code area in and around Hartford —where clinicians incorporated fall risk assessment and management into their practices to those in a control region. Their analysis also showed some 1,800 fewer emergency department visits or hospitalizations; and health care savings estimated at \$21 million over two years.

"The next step is to put [the research] into practice," said senior author Mary E. Tinetti, M.D., the Gladys Phillips Crofoot Professor of Medicine and professor of epidemiology and of investigative medicine, "by making physicians, nurses and physical therapists everywhere more conscious of fall risks ... and of what can be done to prevent falls." ---Michael Fitzsousa



Yale scientists have designed an artificial version of the energy-generating cells in electric eels that could power medical implants.

Yale scientists model artificial energy cells

Chemical engineers design an artificial electrocyte that could be a power source for medical implants.

Researchers at Yale University have created a blueprint for artificial cells that are more powerful and efficient than the natural cells they mimic and could one day power tiny medical implants. Their findings were published online in *Nature Nanotechnology* on September 21.

The scientists began by exploring whether an artificial version of the electrocyte—the energy-generating cells in electric eels—could be designed as a potential power source. "The electric eel is very efficient at generating electricity," said Jian Xu, PH.D., a postdoctoral associate in the Department of Chemical Engineering. "It can generate more electricity than a lot of electrical devices."

Xu came up with the first blueprint that shows how the electrocyte's different ion channels work together to produce the fish's electricity while he was a graduate student under David A. LaVan, PH.D., a former assistant professor of mechanical engineering now at the National Institute of Standards and Technology.

But the scientists didn't stop there. "We're still trying to understand how the mechanisms in these cells work," said LaVan. "But we asked ourselves: 'Do we know enough to sit down and start thinking about how to build these things?' Nobody had really done that before."

Using the new blueprint—based on a mathematical model—as a guide, LaVan and Xu set about designing an artificial cell that could replicate the electrocyte's energy production. "We wanted to see if nature had already optimized the power output and energy conversion efficiency of this cell," said Xu. "And we found that an artificial cell could actually outperform a natural cell, which was a very surprising result."

The artificial cell LaVan and Xu modeled is capable of producing 28 percent more electricity than the eel's own electrocyte, with 31 percent more efficiency in converting the cell's chemical energy—derived from the eel's food into electricity.

While eels use thousands of electrocytes to produce charges of up to 600 volts, LaVan and Xu have shown that it would be possible to create a smaller "bio-battery" using several dozen artificial cells. The tiny bio-batteries would need to be only about a quarter-inch thick to produce the small voltages used to power such tiny electrical devices as retinal implants or other prostheses.

Although the engineers came up with a design, it will still be some time before the artificial cells can be built they will still need a power source. LaVan speculates that the cells could be powered in a way similar to their natural counterparts. Bacteria, he suggested, could be employed to recycle ATP—the molecule that transfers energy within cells—using glucose, a common source of chemical energy derived from food.

With an energy source in place, the artificial cells could one day power a medical implant and would provide a big advantage over battery-operated devices. "If it breaks, there are no toxins released into your system," said Xu. "It would be just like any other cell in your body."

-Suzanne Taylor Muzzin

A gene that helps blood vessels feed tumor growth also aids in brain plasticity

A gene that typically helps rogue blood vessels feed tumor growth also appears to play a helpful role in the body—in brain development. Slight genetic variations in the vascular endothelial growth factor (VEGF) gene sequence correlate with changes in the size of the hippocampus, the brain structure involved in memory, emotion and learning. These changes may be linked to a slew of neuropsychiatric disorders including major depression, schizophrenia and dementia.

"There may be subsets of individuals, for example with mood disorder or bipolar disorder, who have hippocampal differences, and they may be the ones who carry these variations in VEGF," explained Hilary Blumberg, M.D., associate professor of psychiatry, director of the Mood Disorders Research Program and lead author of a paper published online in *Biological Psychiatry* on August 14.

The researchers used magnetic resonance imaging to determine hippocampus volumes in a group of healthy volunteers who had slight differences in the VEGF gene encoded in their DNA. They then employed statistical analysis to identify any correlation between hippocampus differences and VEGF differences. The study findings suggest that variations in VEGF might contribute to individual differences in hippocampus size and structure.

These findings build on pioneering work conducted by one of the paper's co-authors, Ronald S. Duman, PH.D., Elizabeth Mears and House Jameson Professor of Psychiatry, professor of pharmacology and director of the Division of Molecular Psychiatry and Abraham Ribicoff Research Facilities. Duman recently explored VEGF function in the brain and found that it helped new nerve cells grow, specifically in the hippocampus.

Playing a part in neurogenesis is an unconventional role for VEGF. The gene

is known to help cancers grow by laying down new networks of blood vessels that feed malignant cells. Blocking VEGF function is a main goal in the treatment of breast, lung and colorectal cancers, among others.

Joel E. Gelernter, M.D., professor of psychiatry and director of the Division of Human Genetics in Psychiatry, who was examining genetic variations in VEGF, joined Blumberg and Duman for a collaborative effort.

"We're trying to understand at a basic level of cell signaling how disruptions or alterations could contribute to the function of the hippocampus and circuits within the hippocampus, and how these disruptions influence behavior and illness," said Duman. Toward that end, Gelernter offered up his genetic expertise, Duman contributed knowledge about the molecular role of VEGF in the brain from his animal studies and Blumberg brought her brain imaging know-how to bear.

The findings of the current study complement another recent discovery from the research trio. They found that, compared to healthy subjects, adults with bipolar disorder had significantly smaller hippocampus volumes, which were linked to variations in the brain-derived neurotrophic growth factor (BDNF) gene (published online on August 13 in *Neuropsychopharmacology*). Duman predicts that VEGF may behave similarly, in that VEGF variations may make individuals either more or less vulnerable to stress-related mood disorders.

To follow up on this prediction, Blumberg and co-lead author Fei Wang, M.D., PH.D., plan to study VEGF genetic variations in individuals with mood disorders to understand how these gene changes may influence both brain structure and behavior. Ultimately, identifying genetic variants that predispose individuals to mood disorders could pave the way to patient screening for early disease detection and possibly smarter treatments.

-Kara A. Nyberg

et cetera ...

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FIX-IT KIT FOR FAULTY GENES

School of Medicine researchers led by Peter M. Glazer, M.D. '87, PH.D. '87, HS '91, department chair and the Robert E. Hunter Professor of Therapeutic Radiology and professor of genetics, have found a new approach to gene therapy, opening up the possibility of new treatments for inherited hematologic diseases.

In the September 9 issue of the Proceedings of the National Academy of Sciences, the researchers report that they developed genetic "repair kits" consisting of chemically altered pieces of DNA, which bind to human genes and trigger the cell's own repair systems to fix such mutated genes as the one that causes thalassemia, an inherited blood disease. The faulty gene was fixed even in human bone marrow cells, meaning that the genetic repair could be inherited by newly generated blood cells.

The new technique employs small pieces of synthetic DNA that are easy to insert into cells and do not require viruses for delivery. —John Curtis

JUNK DNA AND EVOLUTION

Humans can handle tools and walk upright thanks to a handful of letters in their genome, Yale scientists said in a report published in *Science* in September. Evolution, they suggest, may have been driven not only by changes in genes but also by changes in the sequences that control them.

Some sequences, previously thought of as "junk DNA" because they do not code for proteins, regulate genes that direct human development. With colleagues in California, Singapore and the United Kingdom, the Yale team characterized in mouse embryos a human sequence that had changed since humans and chimpanzees diverged. This sequence drove gene expression at the base of the mouse versions of the primordial "thumb" in the forelimb and the "great toe" in the hind limb.

"The long-term goal is to find many sequences like this and use the mouse to model their effects on the evolution of human development," said James Noonan, PH.D., assistant professor of genetics and senior author of the study.

—Ј.С.

John Kao relies on the "implicit curriculum of medicine" in his career as a consultant on innovation.

How America can get its groove back

A medical school alumnus argues that the nation is not doing enough to foster innovation.

John J. Kao, M.D. '77, M.B.A. '82, does not even mention his medical degree in the biography for his latest book, *Innovation Nation: How America Is Losing Its Innovation Edge, Why It Matters, and What We Can Do To Get It Back.*

Medical school at Yale and a psychiatry residency at McLean Hospital were just starting points for a career that has earned Kao the designation of "Mr. Creativity" from *The Economist*. Along the way he has played keyboards for Frank Zappa; taught at MIT and at Harvard, where he earned his business degree; started two biotech companies; and was production executive on the Palme d'Or-winning film *sex*, *lies*, *and videotape*. Recently he founded a nonprofit, the Institute for Large Scale Innovation.

Despite his distance from hospital corridors, however, Kao said he still draws on what he calls "the implicit curriculum of medicine," which taught him, "You work hard, and no one works harder than you. You take responsibility and make things happen. And you're it: when someone comes into the ER at three in the morning, you're it. I've never forgotten those lessons."

Lately Kao's hard work has involved advising corporate and government leaders around the world on fostering innovation —and warning Americans that they are not doing enough. *Business Week* called his book "scary, insightful, and ultimately very useful," and listed it among the top 10 business books for 2007.

Kao believes that Americans lack a cogent vision of where innovation is taking them, even though half of the world's research and development money is invested within this country. "No country, not even the United States, can afford to be without a strategy," he said. Kao defines innovation as the ability of individuals, corporations and nations "to continuously create their desired future." If the United States wants to chart its own course rather than simply reacting to developments elsewhere, it must foster innovation.

Kao cites Singapore's innovation strategy as instructive. The island nation of 4.5 million has built a huge research complex called Biopolis, paid for talented young people to earn doctorates in the sciences and recruited researchers and advisors from around the world. In his book, Kao quotes former University of



Washington President Lee L. Huntsman, who has called Singapore a "venture capital company masquerading as a government."

Like Singapore, each nation should foster innovation consistent with its national character and endowments, Kao said. Otherwise, he said, "you don't make the best use of your opportunities and resources." The United States, for example, has both strong links between academia and business and a mature venture capital industry willing to take chances on unproven ideas. "And," said Kao, "we have a very forgiving attitude toward what I would call noble failure. ... If you fail in European countries or Asia, typically you're out of the game."

America has also benefited by welcoming immigrants: half of those with doctoral degrees in computer science, for instance, come from abroad. "We'd be stupid to imperil that flow of talent into this country," Kao said. "Many other countries are stepping up to the plate and making their countries highly desirable to immigrant talent."

Kao advises physicians who value innovation to seek skills and knowledge beyond medicine. For instance, he recommends that doctors earn master's degrees in business or in public administration. "These days it's arguably as important to understand how discoveries get into the marketplace as it is to pursue discovery itself. ... The more we can do a variety of things in addition to having our core skills, the more we can contribute to society."

-Cathy Shufro

Bookshelf focuses on books and authors affiliated with the School of Medicine. Send suggestions to Cathy Shufro at cathy.shufro@yale.edu.

BOOK NOTES



Transgenesis and the Management of Vector-Borne Disease by Serap Aksov, PH.D., professor of epidemiology (microbial diseases) (Springer) The author explains the reasons for the resurgence and spread of vectorborne disease. No effective vaccines exist for these diseases. and only limited therapeutic interventions are available to treat them in mammalian hosts. Aksov describes the causes of the spread of these diseases. including habitat change, irrigation practices, atmospheric and climate change, insecticide and drug resistance and increases in global tourism, human traffic and commercial activities. The author also explores the potential of such molecular technologies as transgenesis in developing disease management strategies.

Anemias and Other Red Cell Disorders

by Kenneth R. Bridges, M.D., and Howard A. Pearson, M.D., professor emeritus of pediatrics (hematology/oncology) (McGraw-Hill Professional) This resource provides a practical framework for identifying and managing acute, congenital and chronic anemias as well as other red blood cell disorders. The book describes the principles of anemia evaluation and specific deficiencies in adults and children. Practical Guide to the Evaluation of Clinical Competence by Eric S. Holmboe, M.D., HS '93, professor (adjunct) of medicine, and Richard E. Hawkins. м.р. (Mosby) This guide to outcomes-based assessment in clinical education describes evaluation methods, tools and faculty training approaches for all medical educators. The book can serve as a resource in developing, implementing and sustaining effective systems for evaluating clinical competence in medical school, residency and fellowship programs. The book comes with a DVD.

Autism Spectrum Disorders in Infants and Toddlers: Diagnosis, Assessment and Treatment by Katarzyna Chawarska, PH.D.,

assistant professor in the Child Study Center, Ami J. Klin, PH.D., Harris Associate Professor of Child Psychiatry in the Child Study Center and associate professor of psychology, Fred R. Volkmar, M.D., the Irving B. Harris Professor of Child Psychiatry, Pediatrics and Psychology in the Child Study Center, and Michael D. Powers, PSY.D., assistant clinical professor in the Child Study Center (The Guilford Press) This book synthesizes research on the diagnosis and treatment of autism spectrum disorders in very young children. The authors examine critical research issues and present innovative approaches to assessing social, cognitive, adaptive, communications and sensorimotor impairments in the first two years of life. The book also addresses ways to support families in coping with an early diagnosis and

in becoming effective advocates for their children. The book includes case studies and discusses popular but controversial treatments for these disorders.

Freeing the Human Spirit: A Psychiatrist's Journal

by Louis B. Fierman, M.D., HS '53 (Blue Dolphin) This book consists primarily of 21 case vignettes intended for readers who are involved in or interested in psychotherapy and psychiatric private practice. The book also includes an essay on the development of nondirective therapy, an approach that the author regards as increasing the effectiveness of treatment.

Beating Lyme: Understanding and Treating This Complex and Often Misdiagnosed Disease

by Constance A. Bean, M.P.H. '50, and Lesley Ann Fein, M.D., M.P.H. (AMACOM) The authors offer readers an understanding of Lyme disease, its history and the controversy surrounding its diagnosis and treatment. Topics include what to do after a tick bite, the consequences of misdiagnosis, how to get the best treatment and what to do if insurance won't cover it.

The Woman's Heart: An Owner's Guide

by John A. Elefteriades, м.р. '76, H5 '81, FW '83, the William W.L. Glenn Professor of Cardiothoracic Surgery, and Teresa Caulin-Glaser, M.D. (Prometheus Books) In this guide, the authors focus on the unique factors affecting women's cardiovascular health. Topics include such diseases of the heart as mitral valve prolapse, symptoms of heart disease that women need to know, cardiac tests, medications and surgery, and the ways in which pregnancy and childbirth affect women's hearts.

Current Diagnosis & Treatment: Psychiatry, 2nd ed.

by Michael H. Ebert, м.D., professor of psychiatry, Peter T. Loosen, м.р., Barry Nurcombe, м.р., and James F. Leckman, м.р., the Neison Harris Professor of Child Psychiatry in the Child Study Center and professor of pediatrics and psychiatry (McGraw-Hill Medical) This reference work addresses day-to-day questions about psychiatric illness in both adults and children. It provides information on psychiatry and the law. psychological testing, emergency psychiatry, evaluation of infants, developmental psychology, neuropsychopharmacology, psychiatric genetics, psychoanalysis and the principles of evaluating and diagnosing patients, as well as treatment strategies.

IN CIRCULATION





How to Land a Top-Paying Federal Job: Your Complete Guide to Opportunities, Internships, Resumes and Cover Letters, Application Essays (KSAS), Interviews, Salaries, Promotions and More! by Lily Whiteman, M.P.H. '90

(AMACOM) This book guides prospective applicants through every stage of their federal job search, giving insight into finding openings and negotiating a top salary as well as suggesting techniques for securing promotions.

Educating Individuals With Disabilities: IDEIA 2004 and Beyond

by Elena L. Grigorenko, PH.D., associate professor in the Child Study Center and of epidemiology (chronic diseases) (Springer) This volume discusses the identification and assessment of learning-disabled students today in light of the 2004 Individuals With Disabilities Education Improvement Act (IDEIA). Grigorenko describes the IDEIA in its historical, political and legal contexts and considers practical issues for school psychologists, neuropsychologists, speech-language therapists, policy makers and legal professionals who must deal with special education and learning disability issues on a daily basis.

Medical Humanism: Aphorisms From the Bedside Teachings and Writings of Howard M. Spiro, M.D. edited by Robert E. Kravetz, м.р., FW '65 (The Program for the Humanities in Medicine) This volume gathers many observations, lessons, admonitions, criticisms, witticisms and comments from Spiro's books, essays and papers for the reader's enjoyment and contemplation. Spiro, who served on the School of Medicine's faculty from 1955 until his retirement in 2000, speaks as an experienced clinician and humanist with a broad and visionary outlook on medicine.

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

Expert medical help now available to Connecticut school nurses via new website

School nurse Marcia Wilcox, R.N., didn't have much luck when she used Google to search for information about learning disabilities caused by a rare bone disorder. A teacher at her school in Connecticut needed to know whether a new student would need extra help as a result of the condition.

Wilcox contacted Janene Batten, M.L.S., at the Harvey Cushing/John Hay Whitney Medical Library, who sent Wilcox four journal articles on the condition, "She was able to find something a lot quicker than I would be able to," said Wilcox, the sole nurse for about 400 primary school children. "Sometimes I have time, and sometimes I don't."

This expert help was available on the "Ask a Librarian" feature on a new website for Connecticut school nurses that Batten established with colleagues Jan Glover, M.L.S., and Lynn Sette, M.L.S. They created the site based on a questionnaire they had sent in the fall of 2007 to the nearly 2,000 nurses and nurse practitioners in Connecticut's public schools and schoolbased clinics. Just under half the nurses who filled out the questionnaire said they were too busy during the school day to use the Internet; 44 percent said they lacked knowledge of electronic resources.

The site gives the nurses easy access to 14 databases, including PubMed, the biomedical database for clinicians, and MedlinePlus. Among other resources is a link to the National Library of Medicine's Drug Information Portal, which provides details about 12,000 medications. The site also provides access to librarians who can help with difficult searches, as Batten helped Wilcox.

The librarians developed the site over two and a half years as part of a \$40,000 grant from the National Library of Medicine. They hope that the site, called Connecticut School Nurses Information Resources, can serve as a model for others. In June, the librarians will present a paper about the project at the annual conference of the National Association of School Nurses.

"Unlike a lot of areas of nursing, school nursing is a very solitary practice," said Joan Cagginello, R.N., M.S., the school nurse administrator of the Milford Health Department. The site is "invaluable," she said.

The site's URL is http://www.med.yale.edu/library/ school_nursing/.

-Cathy Shufro

In Circulation focuses on activities at the Cushing/Whitney Medical Library. Send suggestions to Cathy Shufro at cathy.shufro@yale.edu.

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ON CAMPUS



An orthopaedic surgeon fights for diversity in medicine

When Claudia L. Thomas. M.D., HS '80, completed her residency 29 years ago, she was the nation's first black woman to become an orthopaedic surgeon-though somebody had to inform her of her achievement, Thomas, who gave the Southwick Lecture for the Department of Orthopaedics in November, has devoted her career to making up for that oversight, fighting for diversity in both color and gender in medical schools and in doctors' offices. Although there has been progress, she said, there's still a long way to go.

African-Americans make up almost 11 percent of the population but just under 2 percent of orthopaedic surgeons, and only 2.3 percent of orthopaedic surgeons are women. And disparities also extend to treatment: Whites, for example, are 2.4 times likelier to get hip replacements than blacks. Race and gender disparities "are killing people," Thomas said.

Thomas, an assistant professor of orthopaedics at The Johns Hopkins University School of Medicine, led a diversification effort there that increased the number of African-American orthopaedic residents to 32 percent. "When you have a diverse program," she said, "it becomes self-perpetuating eventually."

—John Dillon



How climate change affects public health

In 1967 U.S. Surgeon General William Stewart, M.D., announced that it was time to "close the book" on infectious diseases. There was a hitch to that announcement, said Mary C. Pearl, PH.D. '72, at a talk in November sponsored by The Elihu Club and Tropical Resources Institute: "No one alerted the bacteria and viruses."

The diseases that have since emerged are deadlier and more expensive to fight, said Pearl, president of the Wildlife Trust, a conservation science group. And more than 61 percent of these diseases—including SARS, avian flu, Lyme disease and West Nile virus—have jumped from animals to humans. They're also, she said, the result of human damage to the environment.

In 2006, the Centers for Disease Control and Prevention declared climate change to be the "largest looming public health challenge we face," she said. Among its effects are excessive heat that stresses the heart; pollution that attacks the lungs and heart; water- and vectorborne diseases; more frequent floods and drought; and more environmental refugees, leading to overcrowding, civil unrest and ideal conditions for disease proliferation.

"Emerging diseases originate where there are lots of people living in rapidly changing ecosystems," Pearl said. "Biodiversity is a buffer."

—J.D.



A single-payer system is best Rx in a bad economy

A single-payer system may be the best way to provide health care coverage in the United States, especially when a faltering economy threatens to increase the ranks of the uninsured, an expert said at the Medical Student Council Perspectives on Medicine series in October.

"The employment-based approach is increasingly unworkable," said Gordon D. Schiff, M.D., associate director of the Center for Patient Safety Research and Practice at Harvard's Brigham and Women's Hospital and past president of Physicians for a National Health Program. Roughly 47 million Americans were uninsured in 2007, a figure that will surely rise due to the credit crunch, Schiff said. Half of the nation's 2 million personal bankruptcies were due to medical expenses, even though 76 percent of those filers had health insurance.

It's time "people got over this bogeyman" of government's inefficiency at managing health care, Schiff said. Whereas up to 40 percent of premiums in private plans are spent on nonmedical, largely administrative purposes, Medicare and Medicaid spend only about 2 percent, he said.

While a single-payer plan "isn't perfect," Schiff said, "it is the only approach that ensures universal health insurance for everyone."

—J.D.



Noah Webster—from listing

definitions to tracking disease

Noah Webster, a 1778 graduate of Yale College, is best known for his eponymous dictionaries, but his lexicographical work is far from his sole achievement. Webster was also the largely unheralded "father of epidemiology—indeed, father of all public health in America," said Curtis L. Patton, PH.D., professor emeritus of epidemiology.

Patton, speaking at a celebration marking Webster's 250th birthday in October, said Webster provided "the base upon which modern epidemiology is based, warts and all." The "warts" stemmed from Webster's doubts over the theory of contagion and his belief that meteors and other atmospheric conditions aggravated such outbreaks as the yellow fever epidemics he studied in the 1790s.

"We may laugh at all this, but we didn't have any idea about disease causation at the time," Patton said. Still, Webster knew enough to inoculate himself against smallpox and to warn of the limited benefits of quarantining people.

"He didn't get everything right, but he was conscientious and careful" about gathering data, Patton said. Webster assembled enough of that data to write A Brief History of Epidemic and Pestilential Diseases (1799), which became a standard text in medical schools in the 19th century. —J.D. 15

A tortured soul finds redemption in words

An 1863 graduate of the School of Medicine made his mark as a contributor to the *Oxford English Dictionary* while incarcerated with schizophrenia.

By Jenny Blair





ABOVE After killing a man in London, William Minor was sentenced to an asylum in Broadmoor, where this undated picture was taken.

ABOVE LEFT AND LEFT After his graduation from medical school, Minor performed autopsies on soldiers at Knight Hospital. He published his reports in a book, a copy of which is in the Medical/Historical Library collection.





DAGRADI

ERRY

William Minor contributed to the Oxford English Dictionary for years before his editor learned he was incarcerated in an asylum for the insane.

Some alumni of the School of Medicine make groundbreaking medical discoveries. Some become leaders of medical institutions. William C. Minor, M.D. 1863, also left his mark: he developed schizophrenia, killed a man and became a brilliant linguistic scholar while in an asylum for the insane.

Minor graduated from Yale's medical school, which at that time entailed two years' study, as a qualified surgeon. After caring for wounded soldiers in the Civil War, Minor began to suffer from what would much later be defined as paranoid schizophrenia. In 1868 Minor was admitted to a government hospital for the insane in Washington, D.C., and released from the Army in 1870. During a stay in London that was intended to rest his mind, he shot and killed an innocent passerby while in the grip of delusional paranoia. The British courts judged him not guilty by reason of insanity in April 1872; he was then placed in Broadmoor, an asylum in Berkshire, England, where he began to correspond with the editors of the nascent Oxford English Dictionary. He soon became an invaluable contributor to that effort. The chief editor did not learn until years into their collaboration that the brilliant and hardworking Minor was a mentally ill prison-hospital inmate. Minor's extraordinary life was the subject of Simon Winchester's 1998 bestselling history, The Professor and the Madman, the principal contemporary source of information about Minor.

After graduating from Yale—his handwritten M.D. thesis concerned muscular contraction—Minor performed autopsies on soldiers at New Haven's wartime Knight Hospital. A small book with his detailed and eloquent reports is still available at the Medical Historical Library along with his thesis. Post Mortem Examinations Made at Knight U. S. A. General Hospital reveals haunting glimpses of Minor's time. Most of his autopsy subjects that year had fallen ill in the field with now-unusual lung ailments, including typhus, typhoid pneumonia, pleurisy and "phthisis," or tuberculosis; but others had succumbed to the more familiar "alcoholismus acutus" or even to choking. Minor also published an article in an 1863 issue of Yale's American Journal of Science and the Arts regarding the ability of certain worms to regenerate after being cut apart.

Years later his erudition and exactitude would serve him well in Broadmoor. In the early 1880s-perhaps nine or 10 years into his incarceration—Minor came across a pamphlet that would change his life. It had probably been placed in one of the many books brought to him by his victim's widow (amazingly, the two had become friends). The pamphlet called for volunteers to compile what was then called A New English Dictionary on Historical Principles. Minor threw himself into the task, combing the rare books in his library, then mailing the editors vast numbers of quotations demonstrating the words' meanings and early appearances in English literature. Though Minor was plagued by vivid hallucinations and delusions, the research suited him well and even seemed to serve as therapy. He worked at it with great success for some 20 years.

In his declining years, Minor was considered less dangerous, and his brother arranged his transfer in 1910 to the same hospital in Washington, D.C., where he had been kept 42 years earlier. It was there that he finally received the diagnosis of dementia praecox, an early term for schizophrenia. A year before his death from pneumonia at age 85, he was transferred, still delusional, to a home for the elderly in Hartford. Conn. Minor was buried in New Haven's Evergreen Cemetery in March 1920. His obituary in the Yale press made no mention of his crime, stating instead that while in England "he was found to be mentally deranged ... and [in Broadmoor] he remained ... gradually recovering his mental balance, and devoting his time to scholarly pursuits." Though Minor did not in fact recover his mental health, the fruits of his scholarship done in the throes of schizophrenia can be found throughout the Oxford English Dictionary, a basic reference work in libraries throughout the English-speaking world.

Jenny Blair, M.D. '04, is a physician and writer based in New Haven.



As the medical center grows, so grows the city

The ongoing expansion of the medical center fits in with New Haven's own plans to undo past urban renewal mistakes.

P Care

By Jenny Blair Photographs by Robert Lisak On Saturday, April 19, 2008, a month before she was to graduate from the School of Medicine, Mila Rainof, M.D. '08, left Harkness Dormitory's exercise room and began walking north on York Street. At South Frontage Road, Rainof began to cross against the light. It probably seemed safe: as often happens at that corner, a large truck was blocking cars on the other side as it crossed South Frontage Road on York Street. As the truck cleared the road, though, cars bound for the expressway burst from behind the truck. Rainof dodged cars in two of the three lanes, but the driver of a sports car in the third lane did not see her in time, and Rainof was struck just a few feet from the curb.

Rainof died of her injuries the next day. She was 27.

The intersection at York and South Frontage is one of several around the medical center notorious for close calls. Located beside the busy Air Rights Garage, its signals are some 40 years old, installed at a time when a very different vision of the medical center's neighborhood prevailed. The intersection serves as a transition point between three lanes of city traffic and an on-ramp to the Oak Street Connector, an expressway leading to Interstates 91 and 95. And its traffic flow is frequently impeded by trucks backing in and out of the hospital's loading dock.

A half-century ago, the intersection would have been almost unrecognizable. In the mid-1950s, South Frontage Road was called Oak Street and marked the boundary between the medical campus and the crowded Oak Street neighborhood home to poor Jews and Italian-Americans as well as newly arrived immigrants of every nationality. As part of the ambitious urban-renewal agenda pursued by Mayor Richard C. Lee and funded by government grants, the neighborhood was razed in 1957 to make way for an expressway and two frontage roads. The new roads brought more traffic into the city but isolated the medical campus and separated downtown New Haven from the Hill neighborhood.

PREVIOUS PAGE Once thought to be the epitome of urban planning, the Route 34 Connector never completed its planned path as a highway to towns in the Naugatuck Valley. Instead it divided New Haven, separating the Hill neighborhood from downtown and the School of Medicine from the rest of the university. Now, armed with a fresh vision, New Haven officials are planning to fill in the highway and build mixed-use developments that include retail businesses, office space and housing.

But times have changed. City planners now prefer houses and shops to medians and on-ramps. New Haven has enjoyed an urban renaissance since the mid-1990s, and a series of overhauls proposed by Mayor John DeStefano Jr .-new buildings and roads behind the medical school; garages, restaurants and shopping at Union Station; a redesign of the vast and underutilized Long Wharf area; and a relocation of Gateway Community College from Long Wharf to downtownwill transform the face of the city as completely as Lee's projects did a half-century ago. Bruce D. Alexander, Yale's vice president for New Haven and state affairs and campus development, said of Lee's urban projects, "Unfortunately, as wellintended as those dollars were, they got spent in ways that [mean] we're now undoing virtually all of them. The Coliseum, Chapel Square Mall, the Oak Street Connector-they're all being undone."

A cancer hospital brings change

When Rainof died, plans were already in the works to fix what ails York and South Frontage and 11 other nearby intersections. The catalyst was the Smilow Cancer Hospital. Groundbreaking for the 14-story, \$467 million building on Park Street and South Frontage Road took place in September 2006 after a protracted fight between the city and local unions on one side and Yale-New Haven Hospital on the other. Expected to create 500 jobs and inject \$1 billion into the local economy, it will be the largest health care development in state history, according to Steve Merz, the hospital's vice president for administration. (Previously, the Children's Hospital held that record.)

"The hospital had to expand," said Merz. In the past 10 years, he said, the medical center has seen an increase of approximately 20 percent in the number of patients discharged from the hospital as well as those seen in outpatient clinics. "The demand is unbelievable." In addition to having a higher patient census, the hospital's cancer facilities are spread out over several buildings. Administrators feared that the logistical complexity that presented for patients might be among the problems threatening the hospital's National Cancer Center designation. The result was Smilow, along with two ancillary buildings. At 55 Park Street, a six-story building will house pharmacy and laboratory facilities. And a city-block-sized parking garage called Lot E will be built at 2 Howe Street. Some employees who park at the Air Rights Garage will be asked to park in the new building instead to create space for cancer patients.

Because of the anticipated extra traffic, the streets around the medical center received a significant upgrade. Now a traffic circle, or roundabout, at the end of the Oak Street Connector diverts cars into and out of the Air Rights Garage, keeping traffic off side streets. A loading dock underneath the garage will also direct construction vehicles and delivery trucks directly from the highway into the garage. Twelve pedestrian-friendly traffic lights along the Frontage Road corridors are being installed at intersections, including the one where Rainof died. And an extra lane has been added to the expressway's onramp to discourage drivers from jockeying for position while they merge. The changes will also include such measures as improved pavement markings and signage. "We are doing everything we can to make it as safe as possible for pedestrians at the medical center," Merz said at a review of the plans in August; they are expected to be complete in late spring 2010.

The hospital is no stranger to injury prevention strategies. It co-sponsored the New Haven Safe Streets educational campaign, and its trauma center has been named a member site of the Injury Free Coalition for Kids, a National Program of the Robert Wood Johnson Foundation developed to prevent traffic injuries in the hardest-hit areas of the city.

With a higher percentage of residents who walk to work than any other city in New England, New Haven has much at stake, so many residents will be watching the changes closely. They include Rachel Wattier, a medical student in her fifth year and one of Rainof's classmates. Shortly after Rainof's death, Wattier and other grief-stricken medical students formed the Yale Medical Campus Traffic Safety Group. The group brings together university personnel, aldermen, police, bicyclists, students and other citizens to seek ways to address such neighborhood traffic problems as speeding cars, drivers who run red lights and intersections that are inhospitable to pedestrians.

"A lot of people's behavior, both as drivers and as pedestrians, is due to frustration and urgency," Wattier said. "[Traffic] fatalities are preventable if you reduce speed particularly, and educate people, and improve the infrastructure so that it doesn't allow people to speed comfortably."

If the city has its way, the now-forbidding stretch of parking lots, housing projects and such massive institutional buildings as the School of Nursing, the Tower One/Tower East senior housing and the Doctors' Building between the medical school and the train station will soon be unrecognizable too. Offices, residences, retail shops, and parking structures are planned, as well as a network of new and more pedestrianfriendly streets. Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, says he's pleased by the timing, as the medical school is considering building in that area in a few years. With the street restructuring, he said, the streets will "make more sense."

Perhaps the most drastic change to New Haven's inner city will be the proposed removal of the Oak Street Connector, also known as the Richard C. Lee or the Route 34 Connector. As part of a project called Future Forward, Mayor DeStefano hopes to tear out the expressway-which carries tens of thousands of cars each day into the downtown area and the medical campus—and replace it with an urban boulevard and 10 acres of mixed-use development. Similar changes have taken place in Milwaukee, Portland, Ore., and San Francisco. "We're starting to see market demand to push the highway back to I-95 and bring a street grid back into service," said Michael Piscitelli, director of the city's Department of Transportation, Traffic and Parking. (Alpern applauds the idea, saying that the school looks forward to "being part of a continuous downtown.") The city received a \$5 million federal grant in September to research and implement the change, and studies will begin early this year.

West of the Air Rights Garage, along a corridor where Pfizer built a vast research facility for clinical trials in 2004 and where the Lot E garage will be built, New Haven once again owns what was until recently state land. The city has begun to hold workshops for local would-be retailers as part of its plans to develop what is now mostly a wasteland of grass and parking lots between the two frontage roads.

It wasn't always a wasteland. The Oak Street Connector, the Air Rights Garage and Crown Towers, an apartment building popular with medical students and residents, sit squarely atop what used to be the Oak Street neighborhood. Spreading over II square blocks with 326 buildings, it was either a rank slum or a vibrant inner-city quarter, depending on one's point of view. But by the late 1950s it was marked for destruction.

The city was remaking itself because of the rise of the automobile. A post-World War II jump in car ownership meant that people could live far from work; this change, along with a trucking boom that eclipsed rail freight, meant that cities faced vastly increased motor vehicle traffic even as their downtowns lost residents to the suburbs. New Haven was no exception.

When Lee took office in 1954, he and his city planners thought big. Funded by grants—during the mayor's 16-year administration, New Haven received more federal and state











With very little street-level retail business to draw passers-by, the area around the medical center (6, 7, 10-12) offers few enticements for pedestrians. With both the School of Medicine and Yale-New Haven Hospital contemplating or



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implementing new construction, retail is part of the mix, as are upgrades to a dozen intersections not known for being friendly to pedestrians. Among the changes under way are the Smilow Cancer Hospital (3-5) and two ancillary buildings, a retail corridor along the grassy median that divides Legion Avenue (1-2) and a traffic circle (9) that brings vehicles directly from the Route 34 Connector into the Air Rights Garage (8) and keeps them off side streets.

monies per capita for its urban renewal than any other city in America-the city poured hundreds of millions of dollars into huge projects like the Connector, the Chapel Square Mall and the Coliseum. The dense but threadbare and crime-ridden Oak Street neighborhood and its poor and immigrant residents did not fit the city's new image. Moreover, it seemed to city leaders that bringing in cars would bring life to downtown New Haven. Named for what it replaced, the Oak Street Connector is a 1.1mile spike of concrete that protrudes into the city from the two nearby interstates; it was intended to be part of a larger freeway that would have extended down Route 34 all the way to the town of Derby. The first portion (and, as it would turn out, the last) was completed in 1959. In addition to the loss of the Oak Street neighborhood, Orange and Temple Streets were severed, the Hill neighborhood was isolated, and Yale's medical campus was separated from the main campus. Crossing weedy, glass-strewn sidewalks high above a river of rushing cars has for decades been a fact of life for many people at the medical center.

A new approach to urban planning

The ideas that drove New Haven's city fathers to replace a neighborhood with a freeway were challenged only a few years after it was built. In 1961, Jane Jacobs, an urban activist who would become perhaps the most influential thinker about city planning in North America, published her landmark book, The Death and Life of Great American Cities. In stark contrast to prevailing opinions of the time, Jacobs argued that neighborhoods should be mixed-use; that buildings should vary in age and purpose; that population should be dense; that people walking down sidewalks, sitting on porches and looking out windows are all-important for safety and a sense of community; and that well-intended gargantuan projects actually worsen urban quality of life. Jacobs helped prevent the building of a freeway across lower Manhattan and, later, a similar project in Toronto. Her ideas are at the root of the urban-planning movement known as New Urbanism, whose practitioners include two Yale graduates, Andrés Duany, M.ARCH. '74, and Elizabeth Plater-Zyberk, м.аксн. '74, co-founders of the Congress for the New Urbanism. The movement began in the early 1980s and gave rise to such model towns as Seaside, Fla. Jacobs' thinking also helps to explain why Chicago's Cabrini-Green and similar low-income high-rise housing built in that era later failed so spectacularly.

Inspired by Jacobs' ideas, many area residents have criticized the medical center's infrastructure. Anstress Farwell, M.A. '79, president of the New Haven Urban Design League and a 30-year resident of the city, is one of the most vocal critics. She laments the uninviting nature of the medical campus, with its blank walls, fences along the sidewalk and parking structures. There is little housing and there are almost no inviting street-level retail stores—Cappuccino's, a sandwich café on Congress and Cedar and the Yale Medical Bookstore, are recent exceptions—and no reason for pedestrians to take a stroll. There is little neighborhood feel. As with many features of the city, this situation can be explained in part by the dominance of the automobile.

In recent decades, Farwell said the hospital has reinforced the lack of a street connection "and an over-reliance on single-occupancy vehicles. All those driveways and aprons define the street as related to cars, with pedestrians as a marginalized presence."

As an example, Farwell points to the Air Rights Garage, a joint project of the hospital and the city that bookends the terminus of the Oak Street Connector and arches over York Street. The walk beneath the garage overpass is a bleak and noisy stretch of sidewalk lined by fast-food stores, convenience stores, a pharmacy and parked ambulances. Built in 1982, the garage was intended to be a partial solution to congestion in the surrounding neighborhood and was considered a model for mixed-use development in its time. The Temple Street Parking Garage, built on similar principles, soon followed.

"The Air Rights Garage was really the only thing that made sense," said Philetus Holt, a lawyer who shepherded the Air Rights Garage to completion. A vanpooling initiative by the hospital had had few takers, he said. And the region and city lacked a strong public transportation system. "People did not want to give up their cars."

Merz maintains that the hospital is committed to mixeduse development, pointing out that more pedestrian-friendly features are planned for its newer buildings. "These LEEDcertified, brownfield-redevelopment, mixed-use projects are bringing tremendous economic benefit to the city and medical center," he said.

In recent years, New Haven builders and residents alike have learned from the past. The simultaneous accessions to power in 1993 of both Yale's President Richard C. Levin and New Haven's Mayor DeStefano marked the beginning of a warmer town-gown relationship that would transform the city

yet again. In an era of reduced city prosperity and slipping prestige on the part of the university-it was losing money and faculty, its physical plant was in disrepair, and undergraduate Christian Prince had recently been murdered during a robbery-Yale began to act as a community developer, initiating a homebuyer's assistance program for its employees and buying up distressed retail properties on Chapel Street and Broadway. This change touched off what the media has called the New Haven renaissance. Alexander joined Yale in 1998 after having worked at the Rouse Corp. on such revitalizing projects as Faneuil Hall in Boston and Harborplace in Baltimore. Asked to locate the epicenter of the renaissance, he points to 15 Broadway, where the New York-style 24-hour delicatessen Gourmet Heaven set up shop in 2000 at his invitation. Barnes & Noble and the clothing stores J. Crew and Urban Outfitters soon followed. To encourage lively sidewalk traffic, Yale stipulated that retail tenants remain open until 9 p.m. "We now have life and activity and a very comfortable environment for shopping," Alexander said. "Whenever we have the chance to put shops or restaurants on the ground plane of buildings that are on city streets where the campus interfaces with the community, we try to build in that retail space."

The high-end tenants stayed, and developers elsewhere took notice. According to Alexander, Yale's aggressive retaildevelopment policies have had the unintended consequence of demonstrating to developers that upscale retail and housing could succeed in New Haven. Firms are now bidding on the chance to develop, for example, the Shartenberg site, a planned mixed-use luxury housing development at the corner of State and Chapel streets downtown—a dramatic contrast with the beginning of the Levin/DeStefano era, when the city had to entice developers with perks.

"We have a really good partnership with the mayor, the city administrators and the Board of Aldermen. There's so much power in Yale and the city working together on projects virtually everyone's come to that recognition," said Alexander.

New Haven has also benefited from the biotech boom. Investment in Science Park, a former industrial site, and the refitting of the former telephone company building at 300 George Street with wet labs has ensured that many fledgling biotech companies born of Yale research have stayed in the city.

The replacement of the Oak Street Connector with boulevards is expected to bring more life to an already revitalized downtown. Such a change would reconnect Yale's medical and main campuses for the first time in a half-century. More people may be walking or biking to work, and efforts to reduce motor traffic are under way. Under a process called transportation demand management, the hospital offers incentives to employees not to drive to work, including vanpools and subsidies for public transport. Some 3 percent of employees participate, removing hundreds of cars from the road. The hospital aims to bring the total to 10 percent. The hospital's new buildings will contain street-level retail stores to encourage pedestrian life on the sidewalks. Even the planned Lot E garage, whose primary purpose is to house 845 cars, will contain not only retail and commercial space but also housing. "These are all part of our commitment to responsible, smart development," Merz said. "We're trying to interact with the fabric of the city a little bit better."

The city and the medical center will continue their dialogue, it seems certain, for decades to come. The hospital's satellite Long Wharf Medical Center opened in 2000, in a part of town that will change drastically if DeStefano's plans go into effect. Some employees commute by public transportation, and many more might do so if the commute is simplified. Most of all, the city's plans for Route 34, known as Legion Avenue west of the Air Rights Garage, will directly affect the medical center, and the gradual change of philosophy in urban planning has begun to affect the medical center's vision of itself.

"Does this vision of us just [building new facilities] down Route 34 make sense—having a long corridor of institutional medical services? That was kind of the old vision," said Merz. But the mayor's dream of a dense mixed-use inner city has advantages for the medical center, he said. The reasons for that are straight out of Jane Jacobs: fewer cars; more retail enterprises; a livelier human presence on the sidewalk; and better relations with out-of-town visitors and community dwellers alike, who will see a pleasant downtown rather than a grim expressway as their welcome to the medical center. YM

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Science and culture in a strange land

As the world gets smaller, the Committee on International Health asks whether Downs fellows can find a foreign experience at home.

By John Dillon Illustration by Calef Brown

In 1966, when the medical school first began offering international fellowships to medical and public health students, the typical fellow was a young man getting his first passport. Today's fellows are much more diverse—they are as likely to be female as male, six of the 20 fellows who went abroad in 2008 weren't native-born Americans, and because they came of age in the era of affordable air travel, all have previously visited a foreign country.

"The profile of the student now interested in getting the fellowship has changed," said Kaveh Khoshnood, м.р.н. '89, PH.D. '95, assistant professor of epidemiology (microbial diseases) and chair of the Committee on International Health (СІН), which administers the Downs International Health Student Travel Fellowship. "Forty years ago, it was a lot of white kids from Kansas who'd never been outside the United States."

As the student body changes, the fellowship program faces an emerging challenge: balancing the relative importance of taking a culture versus taking in a culture. As more people come to the United States as refugees or immigrants, do students have to travel abroad to gain foreign experience?

The late Wilbur G. Downs, M.D., M.P.H., a renowned Yale virologist, started the fellowship program with the idea that students should have a chance to do research in the Third World, where their work could do the most good. His experiences in Africa had left him with the deep understanding that poverty, malnutrition and infectious diseases, combined with the corruption often seen in single-party nation-states, lead to grave health consequences. Students would find a Yale mentor and a mentor in the host country, travel somewhere they'd never been—typically to Asia, Africa or Latin America—and conduct rigorous and ethical scientific research. Downs felt that they should immerse themselves in the culture during their stay, but the program's new director, Khoshnood, wants to take a fresh look at what it means to explore a different culture.

A longstanding foreign imprint

Yale alumni, faculty and students have embarked on international health missions since 1834, when Peter Parker, M.D., a medical school graduate and missionary, established the Ophthalmic Hospital in Canton (now known as Guangzhou), the first Western hospital in China. In 1915 the Yale-China Association opened another hospital in Changsha. After World War II, medical school faculty were active in the Atomic Bomb Casualty Commission's epidemiological studies in Japan. When Yale President Kingman Brewster established a program to send students abroad in 1965, Downs secured a \$5,000 grant from the Rockefeller Foundation to launch the fellowship. Since then the program has sent 444 Yale students to scores of resourcepoor nations and has expanded to include nursing and physician associate students as well as those from the schools of medicine and public health.

Downs fellows have studied diseases spread by sand flies in Peru, HIV transmission among drug users in Vietnam, the eating disorder pica among Haitian women of childbearing

age, and post-traumatic stress disorder (PTSD) among survivors of war in East Timor. Though he retired as a professor of epidemiology and public health in 1972, Downs remained committed to the program until his death in 1991. Curtis L. Patton, PH.D., professor emeritus of epidemiology, longtime friend, colleague and traveling companion of Downs, took over as CIH chair until his retirement in 2006.

"We like to think of it as one of our flagship programs," said Paul D. Cleary, PH.D., dean of public health. "We're proud of it, and we try to bolster and promote it."

According to Khoshnood, however, the program needs to adjust to the changing demographics of the students. As an Iranian-American, he personifies the change not just in the program, but also in Yale and in academia, where minorities make up an increasing portion of the student body.

"Global health could mean practicing outside the United States, but it could also mean working with the immigrant population in the United States," he said.

He also thinks that the fellowship needn't be limited to developing countries. "We're not going to send you to the capitals of Europe," he said, but he sees nothing wrong with, say, a Downs fellow working with North African refugees in Spain.

"I tell the students that this is a great project if you have five years and \$500,000, but you have three months and \$5,000."

"What if a student wants to go live among them to see if they have health issues? These scenarios were raised. We decided to table that this year because we couldn't reach an agreement."

And Khoshnood hopes to rethink the program's reluctance to send students to ancestral homelands or countries they already know. "The fact that they are familiar with the culture and language is a good thing," Khoshnood said. "Their research would benefit from this existing knowledge."

One of Khoshnood's students, Farnoosh Hashemian, M.P.H. '05, a 2004 Downs fellow, convinced the CIH to let her travel to her native Iran to study the mental health of Kurds exposed to chemical weapons during the Iran-Iraq war of 1980-1988, noting that she would benefit culturally because she grew up in Tehran and her work was in the rural Kurdish region, a far cry from the life she knew. "Iran is not a homogeneous country," she said. Her work, which found high levels of PTSD among those exposed to chemical weapons even 16 years after the war ended, was published in 2006 in *JAMA: The Journal of the American Medical Association*—a rare feat, Khoshnood said, for a project done in only two months and on a shoestring budget. Tim Mercer, an M.P.H. candidate and 2008 Downs fellow, argued that his two previous trips to Kenya would help him to do research there on the lives of street children. "The more you visit a foreign place, the more you learn about the culture, the more entrenched in it you become," he said.

Patton acknowledged that familiarity can help, but added, "This is not a fellowship to visit aunts or uncles."

The debate continues. Some longtime committee members regard the cultural experience as sacrosanct. According to Herbert S. Sacks, M.D. '52, HS '56, clinical professor in the Child Study Center, and a founding member of the CIH, one goal of the program is to get students out of what he called "academic lockstep."

"We give them an opportunity to start looking at themselves and to reflect about their goals," Sacks said. "What better opportunity to do this but in a contrasting culture? One of the questions is, 'Why do you have to go to Zambia? Why not just go to the ghetto areas in New Haven, Bridgeport or Hartford?' I think it's too easy to go to these areas and work eight hours a day and return to your buddies and the routine of everyday academic life."

Nicole Britten, an M.P.H. candidate whose 2008 Downs fellowship took her to Colombia to study tuberculosis transmission among family members, said a balance is crucial. "It would be wrong to sacrifice scientific rigor for cultural experience, but it would be disappointing to have a rigorous project with no cultural experience," she said. Britten said she was struck by the hospitality of even her most destitute subjects in Colombia. While she required an interpreter for her research, "I have also learned how far body language and facial expressions can go in putting a person at ease when talking about sensitive issues."

Sending students to do research in resource-poor countries also helps them learn to think on their feet in the face of power failures or inadequate water and medical supplies. Erik Hett, M.P.H. '00, who studied disease transmission by tsetse flies in Kenya in 1999, learned to trap the flies by putting jars near water buffalos, whose scent attracted the insects. He and a colleague were extracting DNA from the flies with a centrifuge when the electricity in their village failed, threatening to wipe out their entire day's work. They drove 20 minutes before finding the only working generator in town, at a beauty salon. "There were four hairdressers and a few patrons, and we had a centrifuge on their only table," he recalled.

"We can't imagine the things they have to deal with," Patton said. "Research has been done on the hood of a car. They have to be resourceful."

Safety and culture shock

Each trip by a Downs fellow starts with a research proposal submitted in January and reviewed by a Yale mentor. The Human Investigation Committee then reviews the proposal to ensure that it meets criteria for protecting research subjects. Proposals must also pass muster with institutional review boards in the host country, which provides yet another lesson, this time on how to navigate a foreign bureaucracy. Then the Downs committee interviews the student. "They're not going to get exposed to stressful interviews, but the questions are designed to help them further refine their proposals and clarify their motivations," Sacks said.

Khoshnood notes that the final proposals are often far removed from the original submissions. "I tell the students that this is a great project if you have five years and \$500,000," he said, "but you have three months and \$5,000."

"As young people, we have grand ideas of what we're capable of doing," said Patton.

The awardees are announced in early March; last year 27 students applied for the 20 available fellowships.

The student must also find a mentor at an academic institution or organization in the host country. Often the onsite mentor is found through personal relationships with Yale faculty, and sometimes at the last minute. Khoshnood would like to develop "more sustained and long-term partnerships with a few institutions rather than one-time student projects."

Funding for the fellows' two- to three-month stays comes not just from the Downs fellowship—an endowment that covers travel expenses, visas, insurance, immunizations and medications and provides a modest stipend—but also from the School of Medicine's Office of Student Research, which provides an additional \$5,000 for research expenses. [See "Downs Fellows Cover the World," p. 39.]

In 2008 the CIH had all applicants take the extra step of filling out a one-page statement about how they would protect themselves. They needed to learn not only about the political climate and the history of the country but also whether there were any disease outbreaks that could affect them. They also needed an alternate plan in case their first proposal doesn't work out. "We're not hovering parents, to say the least, but we want to make sure we're not putting anyone in the lion's mouth," Sacks said.

"We put them through the hoops of attending to their own affairs," Patton said. "There are things they may not have thought of when they first applied, like how to protect yourself with words."

Food riots in Haiti last summer diverted nursing student Eden Garber from her plan to conduct nutritional assessments of children there. "It was a bit frustrating," said Garber, who had been studying Creole for two years. After some lastminute revisions to her application, she was off to Uganda.

"Uganda wasn't on my list of places I want to go before I die," Garber said. Still, she fell in love with the country and with the people she worked with.

Safety is not the only issue confronting Downs fellows. Among the elements of culture shock is the realization that they often stand apart from the local population. "I was constantly hissed at in the street and received a lot of attention from men," said nursing student Jessica Pettigrew, who worked with Haitian refugees in the Dominican Republic after the food riots stymied her plans to go to Haiti. "Everyone turned and stared at me, so I was constantly riddled with a certain self-consciousness. When I was doing my fieldwork in the sugar cane fields, there was this assumption that we could heal and help everyone."

Hett didn't enjoy being gawked at while he studied tsetse flies in Kenya, but he recognized its sometimes discomfiting

"We can't imagine the things they have to deal with.... Research has been done on the hood of a car."

perks. "You get treated like royalty for no reason. Just the color of your skin opens up doors," he said. "It puts you in sort of an awkward position. You want to try to get to know people, but I guess you could never cross that barrier to get to *really* know them."

Although Rosha Forman, a nursing student who studied the practices of midwives in Zambia in 2008, found friends quickly in the expatriate community, that wasn't why she'd gone there. "My challenge was to not fall into easy friendships with foreigners, but instead to work at my friendships with Zambians, as those were the people I was coming to get to know," she said.

The complexities of foreign research are nothing new. One of the earliest Downs fellows, Leonard M. Milstone, M.D. '70, HS '77, research scientist and professor emeritus of dermatology, went to Trinidad in 1967 to trap mosquitoes and isolate arboviruses. Because English was the common language and the Caribbean island was not as poor as other developing nations, Milstone said he didn't experience the disorientation other Downs fellows have described. The next summer, however, Milstone traveled to a Native American reservation in New Mexico for a non-Downs research project. Although in both locations he lived in Western-style housing and ate Western food, he found the Trinidad experience less culturally challenging in a way that presages Khoshnood's approach to cultural immersion. "I found the culture on the Indian reservation in New Mexico far more foreign than the culture I experienced in Trinidad," Milstone said. YM

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Online: Yale Netcasts Paul Cleary: The Public's Health: Challenges in the 21st Century





The lost art of the physical exam

Physicians once relied on seeing, hearing and touching a patient to make a diagnosis. Technology has enhanced and sometimes replaced those skills, but many doctors lament their decline.

By Jill Max Photographs by John Curtis

It was a perplexing case: An otherwise healthy 23-year-old man was hospitalized with a life-threatening pulmonary embolism, but doctors had no clue as to what had caused it. The patient underwent every diagnostic study they could think of--CT scan, consultation with a hematologist, a coagulation workup-but all were negative. Mystified, his doctors recommended anticoagulation medication, but it would mean an end to the weight lifting, swimming and running that he enjoyed. Still, because he didn't want to risk another serious blood clot, he was faced with taking anticoagulants for the rest of his life. Luckily, a light bulb went off when Thomas P. Duffy, M.D., examined the young man. Noticing that his patient was very muscular, Duffy, professor of medicine (hematology), had an idea what the problem might be. To confirm his suspicions, he performed a simple test known as Adson's maneuver: With the patient's arm straightened, Duffy placed a finger over the pulse at the wrist and then moved the arm behind the young man's back. When he asked the patient to turn his head, the pulse disappeared; when he looked forward, the pulse returned.

During a preclinical clerkship, "Learning the Physical Exam," in January 2007, Allison Campbell, then a first-year student, peered into the ear of classmate Tyler Dodds. The course takes students through various forms of the physical examination.
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Duffy deduced that the man was suffering from thoracic outlet syndrome, a compression of the blood vessels beneath the collarbone that cuts off blood flow to the arm. Surgery repaired the problem, and a few months later the young man suspended anticoagulation therapy and resumed his workouts.

By all accounts, such maneuvers as the one Duffy performed are becoming a rarity in medicine. Time pressures, an increasing reliance on technology and limited opportunities for bedside teaching have contributed to the demise of the physical exam. "Diagnosis time has been reduced to the time it takes to order an X-ray," said Lisa Sanders, M.D. '97, HS '01, assistant clinical professor of medicine and author of "Diagnosis," a monthly column in *The New York Times Magazine*. "The physical exam will die completely or it will be resuscitated."

Bedside diagnosis in Western medicine

Clinical observation has been a part of medicine since Egyptian, Babylonian, Chinese and Indian physicians began examining the body thousands of years ago. Clinical reasoning and bedside diagnosis first played a role in ancient Greece when Hippocrates began measuring body temperature, evaluating the patient's pulse and palpating the abdomen. But it wasn't until the 19th century that physical diagnosis exploded, with such developments as percussion and auscultation—the tapping and listening that physicians still practice. Sir William Osler, M.D., often described as the father of modern medicine, told his students: "He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all." Medical school faculty continue to dole out such advice to their students today.

Although certain diagnostic skills have been under fire since a paper presented to the American Medical Association in the 1950s discussed the inability of doctors to recognize some clinically relevant heart sounds, during the last two decades or so physical exam skills have fallen by the wayside. "We have technology that allows us to see things we could never see before, hear things we could never hear before. So in a sense technology has expanded our ability to replace a certain sector of the examination with either visual data or other kinds of data that weren't available to us," said Asghar Rastegar, M.D., professor of medicine, who recently stepped down as associate chair of medicine after 15 years. ICU patients, for example, get daily chest X-rays because it's difficult for them to sit up, cough and participate in other maneuvers that are necessary for a complete chest exam.

Although new technologies allow doctors to explore parts of the body that they can't examine any other way, they don't give the whole picture. They can't feel where an abdomen is tender, discern clues from the look on a patient's face or focus on a particular area because of how it feels or what the patient says. "The ability to decide by touching the patient and examining carefully what the appropriate technologies are to diagnose the patient allows technology to become an extension of what I'm doing rather than a replacement," said Rastegar.

The problem with technology arises when doctors rush to order tests without first performing a thorough physical exam. Rastegar noted that patients presenting with a change in mental status in the emergency department frequently undergo a CT scan, which turns out to be normal, only for the doctors to find out later that the patients had overdosed on a prescribed medication. Doctors may be overly reliant on tests because they have confidence in the results; however, tests aren't always accurate. Lyme disease patients, for example, often have the classic signs of rash, fever and muscle aches, yet the blood test is often negative. "Everyone wants to just turn to the back of the book and look up the answer," said Sanders. Tests, she added, are just one more piece of evidence that has to be interpreted by a doctor.

Physical exams and other tests

Doctors like Duffy and Sanders, who are experts in the physical exam and use it regularly, suggest that it can be a valuable guide in deciding which tests to order and letting specialists know where to concentrate their efforts. "However," said Aldo Peixoto, м.D., associate professor of medicine (nephrology) and co-author of Bedside Diagnosis: An Annotated Bibliography of Literature on Physical Examination and Interviewing, "it's important to identify items of the exam that are relevant, ask questions and use technology to answer the questions about how valid and how valuable these maneuvers are." This, he added, allows for optimal use of the physical exam and more selective use of technology. Studies have consistently shown that the patient's history and physical are the most important factors in arriving at a correct diagnosis, whereas lab tests and imaging studies play complementary roles, and that excessive reliance on technology hasn't necessarily improved the quality of patient care.

The tendency to order a series of diagnostic tests, however, may be a symptom of a larger problem—namely, the lack



of time physicians have to devote to their patients. Doctors are under pressure from insurance companies to keep exams brief. Moreover, the 80-hour work week for residents means that attendings have more clinical responsibilities and less time for individual patient care. Ever-shorter hospital stays also affect the amount of time doctors spend with each patient. Those who were trained before 1980 remember that longer hospital stays meant more exposure to patients and unhurried examinations of patients for both residents and physicians. "In my generation a patient might be in the hospital for two weeks and might educate an entire group of students," said Duffy.

Doctors are further removed from their patients because rounds have virtually disappeared from the bedside. Patients are often discussed at "chart rounds" around conference tables due to both a concern for efficiency and respect for patients' privacy. But that change translates to a generation of physicians who have not been as widely exposed to the physical exam and are less accustomed to using it. "In an ideal world you would be expected to use what you find on a physical exam to make clinical decisions, but in practice we very rarely do," said Allison Arwady, M.D. '08, a resident in medicine and pediatrics. Arwady learned the value of the physical exam during a clinical rotation at Mulago Hospital in Kampala, Uganda, between her third and fourth years of medical school. She saw patients given blood transfusions based on their pallor alone, without ever having a complete blood count. "We've lost a lot of skill here for finding and acting on these things," she said.

About 13 years ago, Andre N. Sofair, м.D., нѕ '90, M.P.H. '97, associate professor of medicine, realized that the teaching that had stuck with him most had taken place at the bedside, not at the blackboard. So he initiated weekly physical diagnosis rounds for residents and medical students at Waterbury Hospital. Sessions take place at the bedside with everyone participating, including the patient. Sofair hopes to prepare his students for those times in the middle of the night when they won't be able to ask an attending's advice or depend on technology for a diagnosis. For Samit Joshi, D.O., M.P.H., HS '08, an infectious-disease fellow who did his residency in Yale's primary care program and was in Uganda with Arwady, being able to identify a problem when you don't have access to a CT scanner or transthoracic echocardiography machine highlights why it's so important to gain proficiency in the physical exam. "You have to rely on a detailed neurological or cardiovascular exam or just putting your





Clinical instructor Jon Fessel guided first-year students Isaac Benowitz and Nicole Cabbad in the eye examination in January 2007. The School of Medicine has taken several steps to reinforce the importance of the physical exam—a survey of graduates in 2002 found that many had never been observed taking a history and doing a physical. 34





Instruction in the physical exam starts in the gross anatomy course taken by all first-year students. Working with instructors in the physical exam course, students learn the body's external landmarks that will guide them when working with patients. In the fall of 2008, students Ferrin Ruiz and Anant Vasudevan received instruction from Harry Briggs and Cheryl Walters, director of the physical exam training course.



hands on the patient," he said. "That's faster than getting a test result back."

It's also less expensive. Insurance companies are beginning to clamp down on such costly tests as MRIS unless a physical exam or some other finding justifies them. It's a position that's hard to argue with: it's been estimated that approximately 80 to 85 percent of diagnoses can be reached via the history and physical. But economics aside, there is an intangible benefit to the contact afforded by the physical exam. A physician might spend two hours looking at a peripheral blood smear or one hour discussing a patient's case during chart rounds, but the patient isn't aware of those efforts. "Just putting your hands on the patient—talking to them while examining them—can go a long way in establishing and building a good doctor-patient relationship, because the patient thinks you're more attentive to who they are as a person and what their underlying diagnosis is," said Joshi.

Learning the physical exam

Medical school would seem the logical place to learn the art of the physical exam, but until the late 19th century, most U.S. medical schools included virtually no instruction in clinical medicine. It was in 1893, with the opening of The Johns Hopkins Hospital in Baltimore, that clinical instruction was established as a formal component of medical school curricula. Osler was a pioneer in this area, advocating clinical demonstrations in the third year of medical school and clinical clerkships in the fourth. The current model came into use in the 1950s, with schools moving the clerkships to the third year and the fourth year devoted to hospital rotations. But because these experiences varied so much from institution to institution, clinical education came under closer scrutiny. Between the 1980s and the early 1990s, five major reports focusing on the quality of medical education were issuedthree by the Association of American Medical Colleges (AAMC), one by the American Medical Association and one by the Josiah Macy, Jr. Foundation-all of which highlighted the need to improve clinical skills education.

Curriculum reform has indeed taken place, although it is mostly limited to the first two years of medical school, which has traditionally focused on basic science. In 2002, about 24 percent of U.S. medical schools included formal clinical skills courses, while only 4 percent included such courses in the clinical years. During the last five years, there has been a trend toward integrating clinical skills into the medical school curriculum, to the point where physical exam courses are now required at virtually every medical school in the United States, according to M. Brownell Anderson, M.ED., senior director for educational affairs at the AAMC. "There's a much earlier interaction with patients, trying to make what is being learned in the basic science courses correspond to physical findings," she said. Students at some schools interact with patients in the first few weeks of medical school, while others are assigned to patients or families whom they follow throughout their four years. Medical schools are also using standardized patients (individuals who are trained to follow a scripted clinical scenario), a practice that allows students the opportunity to learn communication skills along with physical exam skills.

Yale is trying to reinforce physical exam skills in a number of ways, especially after a survey of graduates in 2002 revealed that many had never been observed while they took a patient history and performed a physical. "A lot of them felt ill-equipped, specifically in the focused physical exam, focusing in on an area based on a patient's chief complaint or chief symptom," said Chervl A. Walters, м.D., assistant clinical professor of medicine and director of the physical exam training course, in which pairs of students work with an instructor. Students learn how to perform focused exams of organ systems and a sequential head-to-toe, or comprehensive, physical examination. Walters also directs the Clinical Skills Assessment Program begun in 2003, which evaluates students' skills at the end of their third year in 20-minute visits with seven standardized patients. "We have come a long way since the teaching model of presenting cases in a conference room," Walters said. "It's like learning to drive a car. Would you show learners complicated skills once, send them out alone to practice, and then have them report back on how they thought they did?" The students' comments echoed the results of a study Walters published in 2001 that evaluated the physical exam skills of more than 2,000 third-year students from eight medical schools. Most students, the study found, omitted three out of 10 maneuvers critical in evaluating a patient with shortness of breath and chest pain. Walters' course and the assessment program were developed as part of a revamped clinical skills program that also includes medical interviewing and such courses as end-of-life care and psychosocial skills. These courses have moved away from a lecture format to smallgroup, hands-on sessions that give the students an opportunity to practice what they are learning. "We have to work hard to reinforce both the approach to patient care and the specific physical exam skills that are taught in the preclinical years

to show students their usefulness and effectiveness at the bedside," said Richard Belitsky, M.D., deputy dean for education and the Harold W. Jockers Associate Professor of Medical Education. In fact, clinical skills education begins with the first anatomy lab, when students work with instructors from the physical exam course to locate external landmarks that will ultimately help them when they examine patients.

In a cohort study she completed in 2006, Walters found that students in all four years of medical school reliably perform the maneuvers on the comprehensive physical examination. But by the time they enter their clinical years, students aren't as good at employing additional maneuvers that can rule in or rule out specific diagnoses. Teaching and learning, Walters suggests, may be improved by stressing in the third and fourth years the importance of these maneuvers.

During the first two years of medical school, students are a captive audience, but once they begin clerkships and elective rotations, it is harder to incorporate formal clinical instruction into their training. Yale has expanded its clinical skills program into the third year with such courses as "Breaking Difficult News" and "Counseling for Behavioral Change." At the same time, Belitsky is looking for ways to bring more of the skills program into the clerkship, including direct observation of students taking histories and physicals during their clinical years of medical school.

Efforts to ramp up medical students' clinical skills training are well timed. After a 40-year hiatus, the United States Medical Licensing Exam (USMLE) in 2004 added a clinical skills component, which had been discontinued in the 1960s. The one-day test involving 10 standardized patients is meant to reflect a doctor's typical workday and aims to measure the ability of medical students to deal with a variety of patients in clinical settings.

Whether efforts by the USMLE, Yale and other academic institutions will have an impact on reviving physical exam skills remains to be seen. But it's hard to deny the importance of learning those skills and having an opportunity to practice them again and again if they are to remain useful. "Medicine is learned by the bedside and not in the classroom. Let not your conceptions of disease come from words heard in the lecture room or read from the book. See, and then reason and compare and control," Osler told his students. "But see first." YM

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Asghar Rastegar

A master clinician takes on new post

When Stephen J. Huot, M.D., professor of medicine, decided to organize a symposium in honor of ASGHAR RASTEGAR, M.D., he had to fight fierce resistance from the honoree himself. "I got an e-mail, a phone call [asking me not to]," Huot said of the famously humble nephrologist, who is stepping down as associate chair of medicine to serve as co-director of the international health program.

In the end, though, Rastegar acquiesced. The result was a series of tributes from fellow physicians celebrating his life, character and achievements, with accolades ranging from "master clinician" to "humanist extraordinaire."

Huot, who replaced Rastegar as associate chair, traced Rastegar's career from college and medical school in Wisconsin and residency in Pennsylvania to leadership roles at the medical school of Pahlavi (now Shiraz) University in his hometown of Shiraz, Iran, to Yale.

Majid Sadigh, M.D., associate professor of medicine, who trained under Rastegar at Shiraz, said that Rastegar's "boundless energy" was among the reasons the university's prestige skyrocketed in the 1970s. Sadigh then gave a spellbinding account of not only the complexities of practicing medicine in resourcepoor Iran, but also the violence and strife during the Iranian Revolution. Rastegar, a democracy activist, left Iran in 1982 after having been jailed briefly. "Why," Sadigh asked upon seeing his mentor imprisoned, "are they taking a hero to jail?" Two years later, Sadigh and his family were refugees themselves, living in a camp in Rome, when Rastegar secured him an internship in the United States.



At the symposium's close, Rastegar said that he has led a "phenomenally privileged life." When he returns to the city of Shiraz, he said, he always visits the man who ignited his love for reading----a bookseller, now 85, who allowed the 8-year-old Asghar to borrow books. He acknowledged Donna McCurdy, M.D., his mentor at the University of Pennsylvania, who allowed him to "imagine what I could be"; Samuel O. Thier, M.D., former chair of medicine, who urged him to come to Yale; and Frank Bia, M.D., a former professor of medicine, and Margaret Bia, M.D., professor of medicine, who were his interns when he was chief resident in Pennsylvania, and who helped him build a new life in the United States. "My career is indebted to people," he said, "who took a chance on me."



Michael Kashgarian

Pathologist honored with symposium

MICHAEL KASHGARIAN, M.D. '58, HS '63, was the centerpiece of a Yale symposium in October, but the words of praise for him wouldn't have been out of place at a fête in Hollywood or Cooperstown: "a real icon," a "Renaissance man equally at home in town or country" and "a triple threat."

Kashgarian, professor emeritus of and senior research scientist in pathology, was honored for his 50 years at the forefront of research on kidney disease. At Yale he established a diagnostic renal pathology and electron microscopy laboratory that bears his name. Kashgarian was also a pioneer in understanding the process of organ rejection.

Jon S. Morrow, PH.D., M.D. '76, HS '77, department chair and the Raymond Yesner Professor of Pathology and professor of molecular, cellular and developmental biology, and a colleague of Kashgarian for 30 years, said that his "infectious" fascination with renal disease inspired others. "He's been a real icon," Morrow said. "He's profoundly affected the practice of physiology."

Echoing Morrow, former Dean Gerard N. Burrow, M.D. '58, called Kashgarian "really a pathological triple threat" as a clinician, investigator and teacher. A skilled fisherman, wine expert and bridge player, Kashgarian was also a beacon outside the classroom. "The New York City background disappeared into a Yale country gentleman," said Burrow, a friend since medical school.

Although Kashgarian retired in July, he continues to work, completing his remaining research grants. He will also continue to serve as editor in chief of *Yale Medicine*.



Arthur Horwich

Genetics professor named to IOM

ARTHUR L. HORWICH, M.D., HS '78, the Eugene Higgins Professor of Genetics and professor of pediatrics at the School of Medicine and a Howard Hughes Medical Institute investigator, was elected to the Institute of Medicine (IOM), the National Academy of Sciences announced in October. He was one of 65 people recognized last year by the academy for outstanding professional achievements in the fields of health and medicine. Horwich is an expert on the molecular mechanisms of protein folding, a process crucial to the maintenance of life. When proteins misfold, they can aggregate into plaques and lead to a variety of diseases. More than 20 diseases, including such neurodegenerative disorders as Alzheimer disease, have been linked to misfolded proteins.

The IOM election was the second major honor in a week for Horwich, who was also awarded the 2008 Louisa Gross Horwitz Prize by Columbia University for outstanding contributions in biology and biochemistry. Horwich shared the prize with F. Ulrich Hartl, M.D., PH.D., of the Max Planck Institute of Biochemistry in Germany, and Rosalind Franklin, PH.D., who was honored posthumously for her work on the discovery of the structure of DNA. Horwich and Hartl were honored for their contributions to the understanding of the molecular mechanisms of protein folding. E

Benjamin Bunney

Portrait of psychiatry chair unveiled

BENJAMIN S. "STEVE" BUNNEY, M.D., professor emeritus and former chair of psychiatry, returned to Yale in October from his home in coastal Maine for the unveiling of his portrait and a celebration of his 20 years as chair.

"Steve was always a voice of clarity and rationality and steadiness," said William H. Sledge, M.D., the George D. and Esther S. Gross Professor of Psychiatry, recalling a tumultuous time in the department some 21 years ago when Bunney assumed leadership. With Bunney as chair, Sledge said, "we continued to progress and evolve into truly one of the most outstanding departments of psychiatry in the nation and the world."

After remarks by John H. Krystal, M.D. '84, the Robert L. McNeil Jr. Professor of Psychiatry, who called Bunney a "wonderful mentor," the cloth over the painting was removed to gasps and applause.

"This department has been blessed with the most amazing people," said Bunney, "so my job was very, very easy. ... I want to thank everyone here for giving me such a wonderful career."

The portrait by Gerald P. York depicts him sitting on a laboratory table flanked by scientific images, a stethoscope, and a model sailboat ---symbols of his wide-ranging interests. The Sterling Hall of Medicine appears over Bunney's shoulder. In keeping with tradition, the portrait will hang in the departmental offices at 300 George Street alongside those of previous chairs of psychiatry.

Since retiring in early 2008, Bunney has made his home in Newbury Neck, a peninsula in Maine near Acadia National Park.



Roslyn Meyer

Alumna receives Yale Medal

ROSLYN MILSTEIN MEYER, PH.D. '77, assistant clinical professor in psychiatry, is one of five recipients of the 2008 Yale Medal, the most prestigious award given by the Association of Yale Alumni. Meyer is well-known in the New Haven area for her leadership of a wide array of programs and her longstanding commitment to Yale and the university's environs. Most recently, Meyer has supported research and treatment programs at Yale for melanoma. one of the fastest-growing and deadliest forms of cancer. With a gift of \$10 million to the school last spring, she and her husband. Jerome H. Meyer, M.D. '72, HS '77, lecturer in psychiatry, are helping to establish the Milstein **Meyer Center for Melanoma** Research and Treatment, which will enable the development of more investigator-initiated clinical trials and improve Yale's ability to design new treatments for the often fatal illness. Meyer is a trustee of Yale-New Haven Hospital, a patient advocate for Yale's NIH-funded Specialized Program of Research Excellence in Skin Cancer and a co-founder of both New Haven's International Festival of Arts and Ideas and the Leadership, Education, and Athletics in Partnership program. She has served as a member of the Volunteer Council for Women's Health Research at Yale, a board member of the Yale University Art Gallery and a trustee of Yale's Joseph Slifka Center for Jewish Life.



Robert Alpern

Michael Donoghue

Robert J. Alpern. M.D., dean and Ensign Professor of Medicine. received the John P. Peters Award from the American Society of Nephrology (ASN) in November in recognition of his career of research and leadership. The award "recognizes individuals who have made substantial research contributions to the discipline of nephrology and have sustained achievements in one or more domains of academic medicine including clinical care, education and leadership." Alpern, a former president of the ASN, is the second Yale faculty member to receive the award. Gerhard H. Giebisch, M.D., was honored in 2006. Established in 1983, this annual award is named for a leader in the discipline of nephrology who spent his entire faculty career at Yale: Peters was chief of the metabolic division in the Department of Internal Medicine from 1922 until 1955.

Michael J. Donoghue, PH.D., the G. Evelyn Hutchinson Professor of Ecology and Evolutionary Biology, has been named the first Vice President for West Campus Planning and Program Development. Donoghue recently completed a five-year term as the director of the Yale Peabody Museum of Natural History.

Donoghue will work with faculty to develop specific details of new research programs and core facilities and will coordinate the program for library, museum and other initiatives there.

Yale's 2007 acquisition of the West Campus, formerly the Bayer HealthCare complex, is part of a \$1 billion commitment to strengthening science and



John Elefteriades

medical research at the university. The 136-acre facility in nearby Orange and West Haven features 17 buildings with more than 500,000 square feet of state-of-the-art laboratory space, in addition to offices, warehouses and other facilities.

Donoghue joined the Yale faculty in 2000, serving as chair of the Department of Ecology and Evolutionary Biology from 2001 to 2002. He also holds faculty appointments in Yale's Department of Geology and Geophysics and in the School of Forestry and Environmental Studies. Donoghue has served on dozens of scientific committees and has also served on the board of directors of New Haven's International Festival of Arts and Ideas.

John A. Elefteriades, M.D. '76, HS '81, FW '83, the William W.L. Glenn Professor of Cardiothoracic Surgery and chief of cardiac surgery, was given the Distinguished Fellowship Award by the International Academy of Cardiology at the XIV World Congress on Heart Disease in July in Toronto. The award was conferred in recognition of "profound contributions to the field of cardiovascular medicine."

Robert J. Levine, M.D., HS '63, immediate past co-director of Yale University's Interdisciplinary Center for Bioethics, received The George Washington University Distinguished Alumni Scholar Award for 2008. This award was presented at a ceremony in Washington, D.C., in April. Levine is professor of medicine, lecturer in pharmacology and director of the law, policy and ethics core at the Center for Interdisciplinary Research in AIDS. 38



Mazure



Nunez-Smith



Erik Shapiro

developing post-traumatic stress

training and other stressful situa-

disorder during Special Forces

tions and working to develop

preventive strategies that could

benefit civilians as well as mili-

Marcella Nunez-Smith, M.D.,

assistant professor of medicine,

has received the 2008 Herbert

W. Nickens Faculty Fellowship

from the American Association

fellowship recognizes a junior

to remedy inequities in medi-

cal education and health care.

Nunez-Smith is assistant director

of the School of Medicine's Robert

Program, which prepares physician

Wood Johnson Clinical Scholars

leaders to improve the nation's

health and health care system by

translating research into action at

the local, state and national levels.

Erik M. Shapiro, PH.D., assistant

professor of diagnostic radiology

and biomedical engineering, has

received a \$1.5 million Director's

the National Institutes of Health. Shapiro, who arrived at Yale in 2006 and directs the Molecular and Cellular Magnetic Resonance Imaging Laboratory in the Department of Diagnostic Radiology, is developing new ways to enhance cellular and molecular magnetic resonance imaging technology.

New Innovator Award from

of Medical Colleges. The \$15,000

faculty member who leads efforts

tary personnel.



Michael Simons

Edward Zigler

These technical advances will allow scientists to detect, measure and manipulate cell migration in living tissue.

Michael Simons, M.D. '84, a distinguished heart researcher and physician, has been named section chief of cardiovascular medicine at the School of Medicine and Yale-New Haven Hospital.

Simons comes to Yale from Dartmouth-Hitchcock Medical Center, where he served as chief of cardiology, director of the cardiovascular center and the angiogenesis research center, and on the medical center's board of governors. He was also professor of medicine and of pharmacology and toxicology at Dartmouth Medical School. While at Dartmouth, Simons received the department of medicine's Excellence in Teaching Award. Simons previously served as an associate professor of medicine at Harvard Medical School and attending cardiologist at Beth

Israel Hospital in Boston. He was also director of Beth Israel's coronary care unit.

Simons' research interests include fibroblast growth factor signaling in the vascular system, regulation of arterial development, and branching and endothelial signaling.

Edward Zigler, PH.D., Sterling Professor of Psychology emeritus, has been selected as the 2008 recipient of the American Psychological Association's (APA) Award for Outstanding Lifetime Contribution to Psychology. Zigler received the award at the APA annual convention in Boston in August. Known as the "Father of Head Start," Zigler is one of the principal architects of the federal Head Start program and the founder of the School of the 21st Century (21C) initiative.

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sociate dean for faculty affairs and professor of psychiatry and psychology, is the 2008 recipient of the American Psychological Association's Distinguished Leadership Award. This award recognizes innovative research accomplishment and leadership that improve women's lives and advance health outcomes. She is the founding director of Women's Health Research at Yale, which was started in 1998 in response to the need for gender-based research. Mazure was also the 2007 recipient of the Marion Spencer Fay Award, given by the National Board for Women in Medicine.

Carolyn M. Mazure, PH.D., as-

Charles A. Morgan III, M.D., associate clinical professor of psychiatry, has received the Patriotic Civilian Service Award for his service to the John F. Kennedy Special Warfare Center and School at Fort Bragg in North Carolina. Since 1989, Morgan has been researching the factors that increase vulnerability to

Downs fellows cover the world

On topics ranging from nutrition to contraception, students presented their research in October.

For the first half of his 10-week stay in Eldoret, Kenya, last summer, Timothy Mercer just hung out. "I had to earn some credibility and trust," said Mercer, a 2008 Downs fellow who was studying street children in the western Kenyan city. His hanging out paid off. "I never felt so privileged to be let into a social group."

Mercer, a public health student, described his research in an oral presentation at the annual fall symposium of The Committee on International Health-which awards the Downs International Health Student Travel Fellowship. Eighteen students in nursing, medicine, public health and the Physician Associate Program spent the summer conducting research abroad. Two other Downs fellows were planning to travel early this year. The students' projects explored such topics as nutrition and food security in Uganda, barriers to drug treatment in Cairo, emergency contraception in South Africa, circumcision as a means of preventing HIV/AIDS infection in Peru, and patients' attitudes toward health care in Indonesia.

In Eldoret, Mercer's local faculty advisor at Moi University, David Ayuku, M.D., had found that about two-thirds of the city's estimated 2,000 street children go home at night. Most find it easier to get food and money on the street than at home. But on the street they are at high risk for HIV/AIDS infection and drug addiction. "Just being a street child places you at a greater health disadvantage," Mercer said.

Rosha Forman, a student in nursing and midwifery, also spent time getting to know her subjects as she studied how Zambian midwives handled the third stage of labor-the period between delivery and expulsion of the placenta. "You want the placenta to come out and vou want it to come out quickly-otherwise you are at risk of hemorrhage," Forman said, adding that postpartum hemorrhaging is a leading cause of maternal death in the developing world. Forman visited four hospitals and seven clinics and interviewed 14 midwives. "I did a lot of sitting and chatting with the midwives," she said.

Lauren Graber, a medical student, traveled to Kampala, Uganda, at the request of a physician there who was concerned that a local landfill might be the source of high blood lead levels in children. "This is a perfect example of partnered research, answering a question that your host country asks," said Michele Barry, M.D., HS '77, professor of medicine and public health and former director of the Yale/Johnson & Johnson Physician Scholars in International Health Program. Graber, working with five Ugandan medical students and a medical student from Mount Sinai Medical Center in New York, tested 165 children and visited 122 homes. High blood lead levels, the students found, were correlated less with proximity to the landfill than with consumption of canned foods and living along busy roads. "We really need to learn more about how kids are being exposed to lead in Kampala," Graber said.

—John Curtis





TOP Medical student Lauren Graber presented the results of her research on lead exposure in Kampala, Uganda, in October at the annual poster session by Downs fellows. The fellows, students in medicine, public health, nursing and the Physician Associate Program, spend a summer abroad conducting research.

ABOVE At the poster session in the Jane Ellen Hope Building, students reported on their research in Africa, Asia and Latin America. Topics included nutrition and food security in Uganda, barriers to drug treatment in Cairo, the health risks faced by street children in Kenya and tuberculosis transmission in Colombia.

For more on the Downs fellowship, see "Science and Culture in a Strange Land," p. 26.



Auction raises \$32,000 for New Haven-area charities for the hungry and homeless

"Girls' Night Out: Join Drs. Bia, Angoff, Vining and Hansson to enjoy a dinner and the sharing of gossip and wisdom. No Y Chromosomes, please."

A group of second-year students, including auction co-chair Marie A. Rymut, bought this evening with four female faculty for \$650 at the 16th Annual Hunger & Homelessness Auction on November 13. The auction, a traditional blend of fun and charity,



TOP Nancy Angoff, associate dean for student affairs, entered a bid on a blanket made by firstyear medical students.

ABOVE Medical student John Binford also bid on the blanket, to which many of his first-year classmates contributed hand-knit squares.

RIGHT Medical students Nupur Garg and Janice Man, right, looked over a list of items at the silent auction.



raised \$32,000 for several charitable organizations in the New Haven area.

"This is about giving back," said auctioneer Wade Brubacher, a professional from Kansas and father of thirdyear medical student Jacob Brubacher, in his third appearance at the event. "You won't make much money at it, but you'll feel good."

Since its inauguration as an afternoon event in Harkness Auditorium, the auction has expanded to include a week of activities that include a football game between first- and second-year medical students, a performance of chamber music, a panel discussion on hunger and homelessness and film screenings. The week ends with silent and live auctions in Harkness Ballroom and Marigold's.

Among the available items at the silent auction were works of art, services by students and faculty, dinners at homes and restaurants, quilts, jewelry, "Mediterranean Dinner & Debauchery," concert tickets and homemade brownies.

The live auction opened with a perennial favorite, bidding on a bow tie ("Smells faintly of formaldehyde") contributed by William B. Stewart, PH.D., associate professor of surgery (gross anatomy), who has taught the basics of anatomy to first-year students for decades. The tie fetched \$500 from the first-year class in the Physician Associate Program, who outbid their medical school rivals.

This year's proceeds will be donated to Christian Community Action, Columbus House, Community Soup Kitchen, Domestic Violence Services, Junta for Progressive Action, Loaves and Fishes, New Haven Home Recovery and Youth Continuum.

—John Curtis



At annual White Coat Ceremony, students kick off their medical careers

The too students in the Class of 2012 include 51 women and 49 men, 24 graduates of Harvard and Yale, 24 members of ethnic or racial groups underrepresented in medicine and 26 who were born outside of the United States. They were selected from 4,139 applicants, and 46 took time off after college to pursue advanced degrees or research, health care consulting, teaching or volunteer work. "Many have been involved with health care programs in various parts of the country or other parts of the world," said Richard A. Silverman, director of admissions. "This class has real depth of experience and a lot of talent. ... It's a pretty hard class to beat."

At this year's White Coat Ceremony in August, Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, welcomed the new students with thoughts on the Yale system of medical education, whose tenets include no grades in the first two years or class rankings. "Were we trying to make it easier for you as students?" he asked. "The answer is that we expect greater things from you than grades could ever engender. We expect you to become leaders in the medical world of tomorrow."

Frederick D. Haeseler, M.D., director of primary care clerkships and associate clinical professor of medicine, reflected on the art of medicine in the ceremony's keynote speech. Defining medicine as having both human and scientific components, he said, "When physicians connect these two, they are practicing the art of medicine."

Why did students choose the School of Medicine? For Ken Hui, who received



his undergraduate degree at Yale, it was the people. "I thought they'd be really nice and really interesting and that's definitely turned out to be the case since I've been here," he said.

Sounok Sen, a graduate of the University of Pennsylvania, said it was the Yale system, which emphasizes a unique student-faculty collegiality and individual responsibility. "I wanted to use those values to learn medicine," Sen said. Smiling, he added, "I think we have a good group. It'll be a fun time."

—Charles Gershman



TOP The Class of 2012, shown here after donning their white coats in Harkness Auditorium, includes 51 women and 49 men.

MIDDLE Esther Lee donning her white coat at the annual rite of entry into medicine.

ABOVE Almost half the class took time off between college and medical school for research, study, teaching or volunteer work.



Jocelyn Malkin decided to pursue psychiatry, despite barriers to women in medicine at the time. "I just thought [psychiatry] was the living end," she said.

The long view of psychoanalysis

Tracing her professional lineage to Freud, alumni leader Jocelyn Malkin still sees a place for the couch.

As a high school student in Manhattan, Jocelyn Schoen Malkin, M.D. '52, found her calling during a lecture by the prominent psychoanalyst Lawrence S. Kubie, M.D. Though Malkin had long been interested in emotional issues, she said, something clicked that day. "I just thought [psychiatry] was the living end," she recalled, using a colloquialism of the day. Despite the era's formidable barriers to women in medicine, she made up her mind to become an analyst. More than 60 years after that decision, she continues to practice, teach and advocate for psychoanalysis.

Malkin, who was elected president of the Association of Yale Alumni in Medicine in 2007, has long done things her own way. She grew up in Rockaway Beach, N.Y. Both her mother, who had been admitted to law school but discouraged from entering by Malkin's grandfather, and her father, an insurance salesman, strongly valued education.

Studying medicine at Yale, though, had not been in Malkin's plans; it was the unintended consequence of a lark. While an undergraduate at Barnard College, she intended to join her thenboyfriend at Columbia University's College of Physicians and Surgeons. When Yale invited her for an interview, she decided to have some fun. "I dressed like I was going to a football game. ... like an 'import'," she said, using Yale slang from the mostly male era for a woman brought to campus as a date. "Instead of looking like a frump, I ... wore a fur coat." Fritz Redlich, M.D., then head of the Department of Psychiatry and later dean of the School of Medicine, asked her why she would make a good medical student. "I said I had a sense of humor, so I could tolerate an interview like this. ... He loved it!" Yale offered her early admission to the Class of 1951.

Malkin's acceptance may have surprised her undergraduate advisor at Barnard, a female chemistry professor who had advised Malkin during her freshman year to forget about medical school. Fond of dating and partygoing, Malkin had earned subpar grades that year. But she suspects her appearance was also part of the problem. "I didn't look the type," she said. "In those days, you had to look like an old frump, and I was having a wonderful time. I thanked her and never saw her again." Malkin raised her grades, and by the time she was pulling on a fur coat for her Yale interview, she was poised to graduate from Barnard a year early, Phi Beta Kappa and cum laude.

In 1948, at the end of her first year of medical school, after parting from her Columbia boyfriend, Malkin married Myron S. Malkin, PH.D. '52, a former Marine and a senior in Yale College. Unlike most other men she dated, he was thrilled that Malkin planned to practice medicine. The women in his home town, he said, just "sit and play mah-jongg."

The Malkins graduated in 1952, he with a PH.D. in physics and she with an M.D., after taking a fifth year.

In those days eligibility for psychoanalytic training required completion of a medical school internship and a

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psychiatric residency. After completing a pediatric internship, two years of psychiatric residency and a two-year public health fellowship at the Child Study Center, she applied for a position at the newly established Western New England Psychoanalytic Institute in New Haven. The young mother was advised to "wait until you finish having children---you have enough to do."

With no positions open to her in New Haven, the Malkins agreed that any move would have to benefit them both. Malkin, her husband and, by then, two children moved to Philadelphia in 1960, where Malkin began training with the Philadelphia Association for Psychoanalysis and her husband worked on a secret project developing re-entry space vehicles.

Malkin and her husband ultimately settled in Bethesda, Md., where she has practiced, taught and supervised trainees for decades. (While there, Myron Malkin went on to head the United States' first space shuttle program from 1973 to 1980.)

Malkin traces her psychoanalytic pedigree straight back to Sigmund Freud via her Philadelphia supervisor, Robert Waelder, PH.D., who had undergone analysis by Freud, and her Washington mentor, Jenny Waelder-Hall, M.D., who had undergone analysis by Freud's daughter Anna.

Malkin presently chairs a biennial seminar in Aspen, Colo., that is attended by psychoanalysts from around the world. She became active in the Association of Yale Alumni in Medicine in 1996 at her 45th reunion, when she asked why there were no women on the executive committee's nominating slate; she was offered a spot on the committee then and there. Her term as president ends in June.

After a 2006 house fire in which many of her and her late husband's documents and belongings were destroyed, Malkin began preparations to move to New Haven. She expects to arrive this summer and looks forward to continuing active involvement with the psychoanalytic community and the alumni association as well as spending time with her children, Martha and Peter, who live in Westchester County, N.Y., with their families. Malkin's granddaughter is a sophomore in Yale College.

Despite the waning reputation of psychoanalysis and the rise of other therapies, Malkin said the older approach has a place in modern psychiatry. It was, she suggests, greatly oversold in the past.

"[Psychoanalysis] is like an appendectomy. It's a great operation, but you don't do it on everybody," Malkin said. "Analysis is the treatment of choice for certain kinds of patients, and [for them] there's no better treatment." She is concerned, though, about the future of psychoanalysis. "There are fewer and fewer people going into it, and the analytic organizations are lowering standards to be able to do anything to get bodies. ... [But] I think analysis will survive, and should survive, as one important part of the whole armamentarium available for the treatment of mental illness."

—Jenny Blair

From art to medicine and back—how one physician pursued her dreams

As a high school student in New Britain, Conn., **Sophie Trent-Stevens**, M.D. '43, made up her mind to see and paint the far-flung places she saw in exotic landscape paintings at the local art museum. "I thought that if you were an artist you'd go out and see this magnificent scenery," she said. A halfcentury later, after a prestigious medical career, she did.

While the 17-year-old knew that she wanted to become an artist, her mother had other ideas. "Artists starve. You can either be a teacher or be a nurse," her mother told her. Neither option suited Trent-Stevens, so she decided to go to Brown University after a teacher told her she could take art classes while earning her degree there.

At Brown, though, she developed different ambitions. "Marie Curie was a hero at that time. ... I wanted to be another Madame Curie," she said. She spent a summer as an animal technician at a cancer research institute in Maine. Back at Brown, an advisor told her that if she wanted to make her mark in medicine, she ought to pursue an M.D. instead of a PH.D.

During her years at the School of Medicine, the United States became involved in World War II. With servicemen falling ill in the South Pacific, Trent-Stevens decided to pursue tropical medicine. After an internship at Vanderbilt University, she went to the School of Tropical Medicine in Puerto Rico. "They had the mosquitoes, they had the germs, they had the bugs," she said. Art became, for the moment,

Alumni FACES

Early in her medical career, Sophie Trent-Stevens studied tropical medicine in the Caribbean she made house calls in the Virgin Islands by sailboat and on the backs of donkeys.



less important, though she sketched when she could—mostly skulls and patients—and occasionally painted with a mixture of watercolors and white shoe polish.

After a research fellowship in tropical diseases at the National Institutes of Health and a residency in internal medicine in Jacksonville, Fla., Trent-Stevens became chief of medicine at St. Thomas General Hospital in the U.S. Virgin Islands. For nine months, she traveled between St. Thomas and neighboring St. John by sailboat and made house calls on the backs of donkeys. She used an old Navy brig on St. Thomas as a quiet room for a violent patient. She remembers the scene of a suicide by hanging; no one had thought to cut the victim down, which might have saved him. And she remembers seeing a priest in full habit riding on the back of a donkey, with his Bible propped open on the beast's neck. "You saw things that were so different from everyday life that you felt you were living in a dream," she said. The vivid images have remained in her mind for decades.

Trent-Stevens returned to Connecticut in 1949 and pursued a career in internal medicine. She had a private practice as well as an associate professorship at the University of Connecticut, and she served as senior ward physician at a tuberculosis sanatorium in Norwich, the Meriden-Wallingford Hospital and the Veterans Affairs hospitals in Meriden and Newington. She was a founding member of the American Society of Tropical Medicine and Hygiene and played important roles in the American Medical Women's Association and the Pan-American Medical Women's Alliance, among many other organizations.

Once she retired from medicine, though, Trent-Stevens returned to art. In 1982, at the age of 65, she earned a master's degree in art from Central Connecticut State University. (She noticed that the young art students spent a lot of time seeking out free food at campus events, and noted, "My mother was right.") She became a docent at the New Britain Museum of American Art—where she'd seen landscape paintings as a child—and published reproductions of her paintings in *Connecticut Medicine*, the magazine of the Connecticut State Medical Society.

And—at long last—she began to paint the faraway places of her childhood fantasies. She painted her former workplace, the stunningly beautiful island of St. Thomas. She traveled to Bora Bora and painted the Pacific island's mountains and the fish she saw from a glass-bottomed boat. She painted tropical flowers in Hawaii, the Matterhorn in Europe and a harbor in Maine, where her interest in medicine began. The large oils and acrylics adorn the walls of Trent-Stevens' home in Meriden, which she and her late husband, Ronald Stevens, a colonel in the U.S. Air Force, designed and built decades ago. Thanks to medicine, Sophie Trent-Stevens got her wish and became an artist, and she didn't have to starve.

—Jenny Blair

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 or write to Faces, *Yale Medicine*, 300 George Street, Suite 773, New Haven, CT 06511.

NOTES



Pahart Johnson



Robert L. Johnson, M.D., HS '64, and his wife, Barbara Johnson, R.N., have formed a nonprofit organization called Village Relief Foundation to supply medical drugs, books, tapes and instruments to such developing countries as Liberia, Zimbabwe, Myanmar, New Guinea and Chad, Any suggestions for networking for gifts and donations to these countries are appreciated. "We are a hands-on, grass-roots organization and make personal trips to these countries. Next stop: Indonesia."

Leonard

Banco

19705

Leonard I. Banco, M.D. '74, has been appointed senior vice president and chief medical officer at Bristol Hospital in Connecticut. Banco previously spent 12 years at Connecticut Children's Medical Center in Hartford.

Cleve L. Killingsworth, M.P.H. '76, has been appointed to the board of trustees of the MITRE Corporation, a nonprofit organization that provides systems engineering, research and development, and information technology support to the federal government. Killingsworth is chair and CEO of Blue Cross Blue Shield of Massachusetts as well as a faculty member at the Harvard School of Public Health.

Ross M. Tonkens, M.D. '74, has been hired by MDS Pharma Services, a provider of drug



Clove Killingsworth



Ross Tonkens

Holly Ardito



Robert Higgins

Donald E. Ingber, M.D. '84, PH.D. '84. Judah Folkman Professor of Vascular Biology at Harvard Medical School and Children's Hospital Boston, was named director of the new Hansjörg Wyss Institute for Biologically Inspired Engineering at Harvard in October. The institute was founded with the largest individual gift in Harvard's history, a \$125 million donation from Wyss, an engineer who led the Swiss medical device company Synthes for three decades. The institute will bring together engineers, scientists and clinicians across disciplines and will focus on synthetic biology, a "living materials program," and biological control.

Joseph J. Napolitano, M.P.H. '87, PH.D., R.N., was appointed to the Pennsylvania State Board of Nursing in April 2008. Napolitano is a program officer at The Dorothy Rider Pool Health Care Trust in Allentown, Pa., which is committed to improving the health of the citizens of the Lehigh Valley.

1990s

Marc Agronin, M.D. '91, was named the 2008 recipient of the Clinician of the Year Award by the American Association for Geriatric Psychiatry for demonstrating a "profound commitment to the field of clinical geriatric psychiatry." Agronin was also recently promoted to associate professor of psychiatry in the voluntary faculty of the Miller School of Medicine at the University of Miami. Agronin is currently the director of mental health services at the Miami Jewish Home and Hospital at Douglas Gardens.

Jeffrey M. Dembner, M.D. '96, has been named chair of the department of neurosurgery at Hoag Memorial Hospital Presbyterian in Newport Beach, Calif. He continues to be director of Newport Neurosurgery, a multi-subspecialty neurosurgical practice in Newport Beach.

Jean Hee Park, M.P.H. '98, J.D., was married in September to Albert S. Cho, J.D., at Riverside Church in Manhattan. She is a law clerk in Brooklyn to Marilyn Dolan Go, a United States magistrate judge for the Eastern District of New York. Her husband is a partner in the Chicago law firm Kirkland & Ellis and works in the corporate department of the firm's New York office.

20005

David F. Jeng, M.D. '07, HS '08, has begun a three-year ophthalmology residency at Doheny Eye Institute, Keck School of Medicine of the University of Southern California in Los Angeles.

Benjamin Negin, M.D. '04, and his wife, Brina, announced the birth of healthy twin boys, Aaron Isaac Negin and Zachary Evan Negin, on July 20. Negin is a second-year medical oncology fellow at Fox Chase Cancer Center in Philadelphia.

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

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discovery and development solutions based in King of Prussia. Pa., to provide medical oversight for its Phase IIa clinical research activities and to direct the medical and clinical activities of its development and regulatory services. Prior to joining MDS, Tonkens was chief medical officer of Regado Biosciences. a Duke University biotechnology spinoff founded in 2003, and was global head of cardiovascular therapeutics at Ouintiles

1980s

Holly Ardito, M.P.H. '89, has been named director of fee schedule and business configuration at Network Health in Medford, Mass. Ardito previously served as the director of client services for MedVentive, Inc., a health care information technology company also based in Medford.

Inc., a transnational contract

research organization.

Sandra C. Castro, M.D. '84, has been named medical director of the Children's Emergency Department at Johnson City Medical Center in Tennessee. Castro was previously the medical director of pediatric emergency services at Joe DiMaggio Children's Hospital in Hollywood, Fla.

Robert S.D. Higgins, M.D. '85, surgical director of the heart failure and cardiac transplant program and professor and chair of the department of cardiovascular and thoracic surgery at Rush University Medical Center in Chicago, is president of the Organ Procurement and Transplantation Network/United Network for Organ Sharing board of directors. He is serving a one-year term that ends in June.

Franklin H. Epstein, M.D. '47, HS '49, William Applebaum Professor of Medicine at Harvard Medical School, considered one of the giants of metabolism and nephrology, died in Brookline, Mass., on November 5. He was 84 and actively engaged in biomedical research, teaching and clinical care until early October.

During his residency Epstein came under the influence of John P. Peters, M.D., regarded by many as the leading American physician/scientist of that time. Epstein eventually succeeded Peters as chief of the Division of Metabolism at Yale.

After a fellowship at Boston University Medical School in cardiology and a period of time in the United States Army, Epstein returned to the Division of Metabolism and the Department of Medicine. Epstein was one of the first recipients of the Francis Gilman Blake Award for outstanding teaching in the biomedical sciences. In 1972 he moved to head the Thorndike Memorial Laboratory and the Harvard Medical Unit of Boston City Hospital. One year later he joined the Beth Israel Hospital as chair and physician-inchief of its Department of Medicine. He remained at Beth Israel. now the Beth Israel-Deaconess Medical Center, until his death. Epstein was also a longstanding editor of Harrison's Principles of Internal Medicine and of The New England Journal of Medicine.

Epstein received many national and international honors for his accomplishments in nephrology.

Roland H. Ingram Jr., M.D. '60, HS '65, died on July 7 in Atlanta, Ga. He was 73. Born in Birmingham, Ala., Ingram attended the University of Alabama before coming to the School of Medicine. After his

internship at Peter Bent Brigham Hospital in Boston, he spent two years in Japan with the Atomic Bomb Casualty Commission before returning to Yale to complete his training in internal medicine. Following a fellowship in pulmonary diseases at Columbia, Ingram joined the faculty of the Emory University School of Medicine, where he received an award as the outstanding clinical teacher from the Class of 1969. He became professor and director of the pulmonary division at Emory before returning to Brigham Hospital in Boston. He also joined the Harvard faculty, teaching in both the medical school and the school of public health. In 1992 Ingram returned to Emory as chief of internal medicine and director of the pulmonary division for all Emory hospitals.

Frank M. Isbell, M.P.H. '63, died on October 6 in Cooperstown, N.Y. He was 81. Born in Roanoke, Va., Isbell served in the Air Force during the Vietnam War. He earned the Bronze Star Medal for his accomplishments at the onset of the Tet offensive. After returning from Vietnam, Isbell was assigned to the Department of Defense, Surgeon General's Office at the Pentagon in Washington, D.C. He retired from the Air Force in 1970. After serving as an administrator at Yale-New Haven Hospital, Isbell moved to Oneonta, N.Y., in 1973 to become president of A.O. Fox Memorial Hospital.

Michael W. Lau, M.D. '45, died on August 12 at his home in Los Angeles. He was 88. Lau, a urologist, surgeon and former Navy captain, grew up in Bronxville, N.Y. When his father died in 1931, Lau, then 11, helped his mother raise his young sister. As a teenager he washed dishes on a Great Lakes freighter. After graduating from Washington and Lee University in 1941, Lau joined the U.S. Navy before attending the School of Medicine. Upon graduation he joined the Navy Reserve Medical Corps and visited the Far East as the ship's surgeon on the USS Columbus. After his marriage in 1952 he practiced urology in White Plains, N.Y., but soon moved to Beverly Hills. Lau was on the medical faculty at the University of Southern California.

José J. Miranda, M.P.H., M.D. '02, died on September 29 in Fayetteville, N.C., where he was stationed as a major in the U.S. Army. He was 33. Born in Puerto Rico, Miranda graduated from the University of Kansas with distinction in 1997. The same year Miranda entered the School of Medicine on the United States Army Health Professions Scholarship Program. He completed his degree in public health at Harvard in 2001. After graduating from the School of Medicine, Miranda completed an internship and residency in orthopaedic surgery at Eisenhower Army Medical Center in 2006.

George E. Palade, M.D., a Nobel laureate who served on the Yale faculty and founded the Section of Cell Biology, died on October 7 in San Diego of complications of Parkinson disease. He was 95.

Palade earned his Nobel in 1974 for his discoveries about the inner workings of cells, findings that helped launch the field of cell biology. He was a pioneer in the use of electron microscopy to discover and elucidate the functions of such tiny structures as the ribosome.

Born in Jassy, Romania, Palade received his medical degree from the University of Bucharest in 1940. He was a member of the faculty of that school until 1946, when he came to the United States for postdoctoral studies. Palade came to Yale in 1973, and held the Sterling Professorship of Cell Biology from 1975 to 1983, when the section became the Department of Cell Biology upon his retirement as chair.

Palade was elected to membership in the National Academy of Sciences, the Institute of Medicine and the American Academy of Arts and Sciences. In 1974, he shared the Nobel Prize in physiology or medicine with Albert Claude, M.D., and Christian de Duve, M.D.

Palade left Yale in 1990 for the University of California, San Diego, as professor of medicine in residence and dean for scientific affairs.

Rose Papac, M.D., a longtime faculty member of the Section of Medical Oncology in the Department of Internal Medicine and one of the early female pioneers in medical oncology, died on May 10 of cancer. She was 80. Born in Montesano, Wash., Papac attended Reed College in Portland, Ore., and studied chemistry at Seattle University, where she graduated summa cum laude. In 1949 she was one of the first women to be admitted to St. Louis University Medical School, and she became the first woman to complete an internship in the department of medicine there. In 1954 she moved to Stanford University to complete her internal medicine residency. It was there that she developed her interest in and passion for oncology; following her residency, she was the first American to take an oncology fellowship at the Chester Beatty Institute in London. She continued her fellowship at Memorial Sloan-Kettering



Cancer Center in New York City. In 1963, she joined the Department of Medicine at Yale, where she stayed until her retirement in 2006. Papac was one of the first women to receive tenure in the School of Medicine and the first woman to be awarded tenure in the Department of Medicine. She played a pivotal role in developing contemporary concepts of cancer chemotherapy.

Marc G. Pypaert, PH.D., director of Yale's Electron Microscopy Core Facility and a research scientist in the Department of Cell Biology. died at Connecticut Hospice on July 28 of brain cancer. He was 45. Pypaert had a diverse and prolific scientific career, developing a high level of expertise in membrane cell biology and, in particular, in electron microscopy of a variety of cells, especially those undergoing mitosis. He was an enthusiastic and creative photographer who exhibited his work at local galleries in the City-Wide Open Studios program. Born in Ath, Belgium, Pypaert received his bachelor's degree in zoology in 1985 from the Facultés Universitaires Notre-Dame de la Paix in Namur, In 1991, he received his PH.D. in biochemistry from the University of Dundee in Scotland. Following postdoctoral work in the United Kingdom, Switzerland and Belgium, Pypaert was recognized as one of the world's leading experts in quantitative immunoelectron microscopy. He was recruited by Yale in 1999. He expanded the scope and technical capability of the Electron Microscopy Core Facility, a component of the Yale Center for Cellular and Molecular Imaging.

J. Murdoch Ritchie, PH.D., Eugene Higgins Professor Emeritus of Pharmacology, died on July 10 in Hamden, Conn., after a long illness. He was 83. Born in Aberdeen, Scotland, Ritchie graduated with a degree in math and physics from the University of Aberdeen in 1944. During World War II, he served on a team that was instrumental in the development of radar. After the war. Ritchie earned another bachelor's degree. in physiology, from University College London (UCL) in 1949. a PH.D. in biophysics in 1952. and a D.SC. in biophysics in 1960. While at UCL he met and married his wife, Brenda, a physiologist. In the early 1950s Ritchie joined Alfred Gilman's department of pharmacology at Albert Einstein College of Medicine. In 1968 he came to Yale as chair of pharmacology. Ritchie made several major contributions to improved understanding of the conduction of impulses in peripheral nerves, in particular the distribution of sodium and potassium channels in both myelinated and unmyelinated fibers. This research led to a better understanding of the disease process involved in multiple sclerosis.

Daniel Rowe, M.D., of Hamden, Conn., professor emeritus of pediatrics and of epidemiology and public health and founding director of the Yale Health Plan, died on July 8. Rowe was a 1948 graduate of Thomas Jefferson Medical College in Philadelphia and served in the Army during World War II and the Navy during the Korean conflict. Rowe came to the School of Medicine as the director of pediatric outpatient services in 1966. While director he developed the domestic abuse response team program for the detection and reporting of child abuse, which is still the model

for child protection in the United States. He was the recipient of the Francis Gilman Blake Award for excellence in teaching in 1968. Rowe was named a full professor of pediatrics in 1970, the year he also became director of Yale University Health Services. The Yale Health Plan was the first university HMO in the country.

Julian A. Sachs, M.D. '46, died on September 1, in the emergency room at the Hospital of Central Connecticut in New Britain, where he had worked for 25 years. He was 86. Sachs was one of the hospital's original emergency room physicians in 1968. He retired in 1992. He was a veteran of the U.S. Army, serving as chief of radiology at Fort Totten General Hospital in New York City and as a transport surgeon on a Victory ship.

Gaston Leonard Schmir, PH.D. '58, professor emeritus of molecular biophysics and biochemistry, died on July 2 of Parkinson disease. He was 75. Schmir was born in Metz, France, in 1933 and spent his childhood in hiding during World War II as his father sought safe havens for his Jewish family. He arrived in the United States in 1946 and Joined the Yale biochemistry faculty in 1960. His research emphasis was in the area of enzyme mechanisms and related physicalorganic chemistry.

Cornell Scott, M.P.H. '68, chief executive officer of the Hill Health Corporation in New Haven, died on August 25. He was 73. Scott came to the Hill Health Center in 1968 as director of training and education and became executive director in 1972. His 40-year tenure was marked by the steady development of sites, services and programs for the low-income population of the New Haven area. He received the National Association of Community Health Centers Lifetime Achievement Award in 2002 for his "lifelong dedication and exceptional service to the American people."

Florence **S. Wald**, R.N. '41, M.N., M.S. '56, dean emerita of the Yale School of Nursing and founder of hospice in the United States, died on November 8 at her home in Branford, Conn. She was 91. Born Florence Schorske in New York City in 1917, Wald graduated from Mount Holyoke College in 1938. After World War II, she became an instructor in the school of nursing of Rutgers University.

After joining the faculty of the School of Nursing in 1956, Wald served as the school's fourth dean from 1959 to 1966. She married Henry Wald, an engineer, in 1959. She is credited with bringing the hospice movement to the United States from England and establishing the first American hospice in Branford in 1971.

A world-renowned leader in nursing research, Wald was awarded an honorary doctor of law degree from the University of Bridgeport in 1967, an honorary doctor of humane letters degree from Mount Holyoke in 1978 and an honorary doctor of medical sciences degree from Yale in 1995.

SEND OBITUARY NOTICES TO Claire M. Bessinger, Yale Medicine, 300 George Street, Suite 773, New Haven, CT 06511, or via e-mail to claire.bessinger@yale.edu Follow-up



One year later, transplant program is thriving

On a crisp fall afternoon, Sukru Emre, M.D., chief of organ transplantation and immunology, had just looked in on a 7-month-old boy recovering from a lifesaving liver transplant—the surgeon's 51st such surgery in less than 14 months. "He's doing very well now and hopefully will go home soon," Emre said.

Since Emre came to Yale last year to revitalize the organ transplantation section [See "Putting the Fire Back into Yale's Transplant Program," Autumn 2007], he has also raised the number of kidney transplants-the section has done 101 in the past year, the highest number in its history-while the liver program boasts a best-in-the-nation survival rate of 100 percent six months after surgery. Although infection rates after transplants are typically 17 to 25 percent, at Yale the infection rate is less than 3 percent. "The credit should go to the nurses working on those units," said Emre. Emre and his team were also the first in Connecticut to perform such cutting-edge liver transplant surgeries as split- and living-donor liver transplantations in both adult and pediatric patients. In split-liver transplant, a single liver is sectioned to serve more than one recipient. Both procedures allow surgeons to overcome the shortage of organs from deceased donors. According to the federal Department of Health and Human Services, 19 people across the United States die each day awaiting transplants. To encourage organ donations, Emre gives talks most weekends at hospitals and events sponsored by donorship foundations, an outreach that has increased the number of organs available and identified Yale as a leader in transplant surgery.

Emre believes strongly in the team concept; he lists individuals and departments throughout the hospital and medical school who contributed to his section's renaissance. He also thanks team members' families for making their success possible. The section has grown with the addition of six physicians, six nurse-coordinators and a nurse-manager. Along with growth has come a reorganization that has increased the section's responsiveness to patient needs, Emre said.

-Colleen Shaddox

Archives 50 AND 25 YEARS AGO



Hunter Radiation Therapy Center Dedicated —Alumni Bulletin January 1959

"The new Hunter Radiation Therapy Center was dedicated on Friday afternoon, October 10. Officials of the University and of the Grace-New Haven Community Hospital, faculty, staff, and guests attended the dedication ceremony, which was held in Fitkin Amphitheater with Dean Lippard presiding.

"The program was opened with a welcome by George S. Stevenson, president of the hospital. President A. Whitney Griswold spoke briefly on "The Medical Center and Yale." This was followed by the introduction of Mr. Robert E. Hunter of Santa Barbara, California, who had made a generous gift to Yale for this building. Mr. Hunter is a Yale alumnus, Class of 1911 (Sheffield Scientific School). The new center is named in memory of his parents, the late Mr. and Mrs. Edward S. Hunter. ...

"The four-story, brick-faced structure has its entrance on Davenport Avenue, and corridors connect with the adjoining hospital units. High-voltage equipment is below ground level. The twomillion electron volt Van de Graaff deep therapy machine was given by the Donner Foundation. Three other radiation machines of lesser voltage are also available, and there are facilities for eventual inclusion of additional high-voltage equipment which may be developed in the future."



Program for Humanities in Medicine —Yale Medicine Spring 1984

"The School of Medicine recently received a grant from the Connecticut Council for the Humanities in support of a new program for humanities in medicine. Directed by Dr. Howard M. Spiro, professor of medicine, the program is presenting a series of twelve semimonthly lectures throughout the spring and fall to bring together scholars in the humanities and members of the medical profession in discussions about the influence of the arts and letters on medicine and health.

"Speakers include Dr. Robert Coles, professor of psychiatry and medical humanities at Harvard University; Arnold Rampersad, professor of English at Rutgers University; Arthur Caplan, associate for the humanities at the Hastings Center; and Dr. Martin Carey, associate professor of medicine, physiology and biophysics at Harvard University. They will discuss topics as diverse as the physician as a writer; the effects of health and well-being on art and visa versa; ethical issues in organ transplantation, and creativity and illness.

"The purpose of the series, according to Dr. Spiro, is to encourage medical students and professionals to expand their definitions of health and disease through a better understanding of the cultural and intellectual influences on health and well-being, as well as to stimulate scholars in the humanities to take a greater interest in health related issues. The lectures are open to the public without charge."

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A LIFELONG LOVE OF YALE

The relationship between Nicholas P.R. Spinelli, M.D. '44, and Yale began in 1937, when he entered Yale College as a freshman. This early acquaintance blossomed through his years at the School of Medicine; in his career as a physician and educator; in his role as a leader of alumni; and in his later years, in philanthropy.

Those who knew him say the same thing: No one loved the Yale School of Medicine more than Nick Spinelli. That love was expressed in many ways, most recently with a \$4.5 million bequest that will support a professorship in neurology and a scholarship fund for medical students.

Spinelli, who died in November 2007 at the age of 86, endowed the faculty position in the name of Harry M. Zimmerman, M.D., a neuropathologist during Spinelli's student days who became the founding director of the Albert Einstein College of Medicine in the Bronx, N.Y. Spinelli funded the scholarships in keeping with his long practice of helping medical students. "He used to worry about how much it cost students to become a doctor, and said he didn't know how they did it," said his sister, Viola J. Spinelli, M.P.H. '65.

Spinelli graduated from Yale College in 1941, began medical school later that year and, along with his classmates, was inducted into the Army. Upon his graduation in 1944, Spinelli served as an Army physician in Germany. In 1968 a heart condition forced Spinelli to give up his career as an internist, but he continued working as director of medical education at Bridgeport Hospital. He retired at age 65 and served as alumni director at the School of Medicine from 1985 to 1990.

He received numerous awards, including the Yale Medal, the university's highest honor, and both the Distinguished Alumni Service Award and the Peter Parker Medal from the School of Medicine. But no award could match the satisfaction Spinelli received from his interactions with students and residents, said his sister Viola.

—Michael Fitzsousa



Nicholas Spinelli sponsored many students at the medical school, including several from Thailand. Kanya Suphapeetiporn graduated from the medical school in 2002 with both an M.D. and a PH.D. After a residency in Brooklyn, N.Y., she returned to Thailand. vale medicine 300 george street, suite 773, New Haven ct 06511

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yale Medicine

Dean signs on for another five years

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Rock 'n roll, genes and mice When scientists become artists

spring 2009

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200 Years of Medicine at Yale

Cast your votes for the most significant events and personalities of the school's first two centuries

ON THE COVER In 1895 medical students posed for a photo at an unknown location. Some wrote the year on the soles of their shoes with chalk, while others showed macabre humor by posing with skulls.

Photograph courtesy of Cushing/Whitney Medical Library

INSIDE COVER When the Class of 1954 posed for a photo on Match Day in the Historical Library, the student body largely comprised white men, although women had been in the school since 1916. In that year Louise Farnam, Helen Scoville and Lillian Nye became the first women to gain admission to the medical school. One thing, however, stood in their way-the lack of proper bathroom facilities. Farnam's father, Henry Farnam, a professor of economics at Yale College, paid to provide "suitable lavatory arrangements." With a few exceptions, until the 1960s no class counted more than 10 percent women among its members. The Class of 1998 was the first at the School of Medicine with more women than men. In almost every year since then, women have outnumbered men and become a ubiquitous presence on the wards and in laboratories.

Photograph courtesy of Cushing/Whitney Medical Library

INSET At Commencement in 2008, not only were there more women than men in the graduating class, but the makeup of the student body reflected broader societal changes, with more students from racial and ethnic minorities and, in an increasingly commonplace sight, parents who brought their children to the ceremony.



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200 Years of Medicine at Yale

Cast your votes for the most significant events and personalities of the school's first two centuries.

How a rock 'n' roll scientist built a better mouse By inserting human genes into mice, Richard Flavell and his team

are creating a mouse with a working human immune system. By Michael Fitzsousa

When scientists become artists

An ongoing <mark>exhi</mark>bit of interesting scientific images raises the question of what constitutes art. *By Jenny Blair*

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Make premed courses more relevant

One of the benefits that are sure to result from making the premed curriculum more relevant to medical practice ["Reform of Premed Education Under Way," *Yale Medicine*, Winter 2009] is that it will attract more students into primary care.

Most medical schools are research-based and naturally favor students with outstanding aptitudes in basic science. This has produced many advances and well-trained specialists, and society has benefited immensely. The focus on specialization, however, has also led to a serious shortage of primary care doctors. The lack of access to primary care has prompted policymakers to consider giving authority to nurse-practitioners to practice some aspects of primary care independently.

In my 34 years of practice as a primary care doctor, I have found almost no use for the intense exposure I had in premed to calculus, organic chemistry, physics, invertebrate biology and physical chemistry. This is not to say that these courses were worthless, but they could have been abbreviated and simplified.

I can remember several students in my premed class who struggled through the basic sciences. Their grades in the sciences were average and they did not do well on the MCATS. Turned down by medical schools at home, many attended foreign medical schools, as I did.

The point is that the move to make premed courses more relevant is a good one. Perhaps students with the abilities to be good general practitioners will not be weeded out and eventually the primary care physician shortage will be corrected. Edward J. Volpintesta, M.D. Bethel, Conn.

Thanks for the photos from a fan of the big dig

My 2-year-old son would like to thank you for the wonderful photos in your Winter 2009 issue ["As the Medical Center Grows, So Grows the City," *Yale Medicine*, Winter 2009]. He is a BIG fan of "dig, dig" and the ongoing projects at the medical center have given him much enjoyment over the past year.

Sandra J. Bishop-Josef, PH.D. Assistant Director, Edward Zigler Center in Child Development and Social Policy; Associate Research Scientist, Child Study Center, Yale School of Medicine

Article on physical exam recalls Klatskin's skill

I just received the Winter 2009 edition of *Yale Medicine* and enjoyed a number of articles, including the roast of Yale's "pathological triple threat." Both I and my father, Wilbur G. Downs, M.D., M.P.H., much enjoyed our acquaintance with Michael Kashgarian, M.D. '59, HS '63.

There was considerable mention of the Wilbur Downs International Health Travel Fellowship Program, as well as a nice piece about Curtis Patton, PH.D., professor emeritus of epidemiology.

I myself am a fan of the Oxford English Dictionary and I've read *The Professor and the Madman*. ... and so I enjoyed the article on William Minor.

Additionally, as a practitioner of ER medicine, I am acutely aware of how technology has served to erode our physical exam skills. The article by Jill Max was very apropos and I admit I had forgotten about the Adson maneuver. One of the professors of my era, Gerald Klatskin, M.D., could percuss out a liver edge or a heart border such that a student across the room could hear it.

Monty Downs, м.р. '70 Караа, Hawaii

Writing award for Yale Medicine editor

In February we learned that John Curtis, managing editor of Yale Medicine, had received the Award for Excellence in General Staff Writing from the Group for Institutional Advancement of the Association of American Medical Colleges. Curtis received the award for his feature article in the Winter 2008 issue, "On the Wards in Uganda." To report on an ongoing collaboration between Yale and Makerere University in Kampala, Curtis spent two weeks shadowing Yale attendings, residents and medical students as they worked alongside Ugandan colleagues at the governmentrun Mulago Hospital. He also accompanied them on field trips to camps for internally displaced persons in northern Uganda and to the fishing village of Kasensero on Lake Victoria, where Uganda's AIDS epidemic began.



Online: Yale Netcasts Additional content for articles in this issue of Yale Medicine is available online at iTunesU, or by pointing your browser

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vale medicine

Alumni Bulletin of the Yale University School of Medicine Spring 2009, Volume 43, No. 3

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Yale Medicine is distributed to alumni, faculty, students and friends of the School of Medicine, as well as to leaders in Yale University alumni activities.

Abbreviations commonly used in *Yale Medicine* include Hs to denote the final year of residency for house staff, FW for the final year of a fellowship and YNHH for Yale-New Haven Hospital.

Postal permit held by Yale University, 155 Whitney Ave., New Haven, CT 06520

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World events bring change to Yale and to Yale Medicine

Changes—some long-planned, others arising of necessity—are in the air for *Yale Medicine*. For more than a year we've been contemplating a redesign of the magazine. In the nine years since the last redesign, as some sections and pages have begun to show their age, we have seen a need to bring variety and flexibility to them. Our first step will be to survey our readers to ask what you like—or don't like—about the magazine. Many of you should expect to receive a survey, by mail or e-mail, in the coming weeks.

Then came word last December that the global economic crisis had reached the university, reducing its endowment by a quarter and requiring cuts in spending. In February came another announcement—the crisis was more severe than anticipated and belts would have to be pulled even tighter.

The School of Medicine is not immune to these events. To meet requests to reduce spending, we are scaling back on *Yale Medicine*. We are still looking at ways to cut back, but options include shrinking the magazine from our current size of 48 pages for the winter and spring issues and 64 for the autumn issue to a standard 32 pages for all three issues. Or we may cut back from three issues a year to two. These changes will drive our redesign; and sadly, we'll see the reduction or elimination of certain pages and sections.

Despite these changes we will continue to produce what we consider a first-rate publication, with compelling stories about the medical school and the issues and events that affect it. We hope that *Yale Medicine* will continue to engage you and help you to maintain your ties to the School of Medicine.

John Curtis Managing Editor

SECOND OPINION BY SIDNEY HARRIS



A first term marked by progress and growth

With kudos from Yale's president and his peers, Robert Alpern signs on for another five-year term as dean.

When Robert Alpern was appointed dean in 2004, his vision for the School of Medicine was to build programs in education, research and clinical care to rival the best in the world. "Yale already has many outstanding programs in these three arenas that are likely among the best, but no medical school is perfect in all aspects," he said in an interview from Dallas, where he was then dean of the University of Texas Southwestern Medical School. "We will identify our priorities for program improvement and then move forward."

Coming to Yale with a reputation for being at once easygoing and ambitious, the new dean rallied faculty, set priorities and vowed to build an already formidable institution into something even greater. In the dozen years preceding his arrival, the medical school had slipped from third to 11th in the annual *U.S. News and World Report* survey and from third to eighth in funding by the National Institutes of Health. By March 2009, however, it had moved back up several rungs on both lists.

While Alpern discounts rankings as often-flawed indicators of quality, he recognizes that they reflect how the school is perceived. Much more important are the real accomplishments of the faculty; by that yardstick, he said, the school is "soaring." He credits his leadership team and says that the real proof of quality can be seen in the creation of new programs that lift Yale above its peers. Among them are multidisciplinary groups focused on cellular neuroscience, neurodegeneration and repair, stem cell biology, human and translational immunology, and cell biology. The school has also seen continued growth in areas where it already excelled, such as genetics, immunobiology and internal medicine.

Alpern has also expanded the clinical practice and the school's capacity to conduct clinical research. In 2006, the School of Medicine won a landmark grant under the NIH Clinical and Translational Science Awards (CTSA) Program. The \$57 million grant—Yale's largest ever—has been critical in building infrastructure linking the school's research base to the clinical practice.

One of the clinical initiatives is a new transplant program with outstanding liver and kidney components. A new chief of cardiology arrived last summer and is building the section's strength in interventional cardiology, heart failure, electrophysiology and basic research. The Smilow Cancer Hospital is set to open in the fall, and in February Alpern named a new director for Yale Cancer Center. Five biomedical institutes and three new core facilities are planned for the West Campus.

In announcing Alpern's second term in February, Yale President Richard C. Levin said that faculty and staff are enthusiastic in their support for the dean. Levin went on to say that Alpern had "transformed the school's relationship with Yale-New Haven Hospital (YNHH), a profound change that will have a lasting impact on the school's clinical mission."

"To take a school as good as Yale and make it better is exciting, and we've come a long way," Alpern said. "The reason I've signed on for another five years is to continue that ascent."

—Michael Fitzsousa

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Online: Yale Netcasts Robert Alpern: Vision for the School of Medicine

In his five years as dean, Robert Alpern has overseen an expansion of the medical school's space, the addition of new programs and an increase in grants and contracts from the National Institutes of Health. In February, he was appointed to a second five-year term. "To take a school as good as Yale and make it better is exciting, and we've come a long way," Alpern said.

Yale obesity expert lauds New York tax dedicated to health programs

When Kelly Brownell, PH.D., published an op-ed piece in *The New York Times* in 1994 pioneering a tax on junk food, he became the focal point of a nasty controversy. Rush Limbaugh lashed out at the notion of the government telling people what to eat, and Brownell accumulated "a very thick file of angry letters. I got things from people saying, 'We know where you live and we're going to drive you right into the New Haven Harbor,'" Brownell said.

But he stood firm, and this year he has seen a glimmer of hope in New York Gov. David Paterson's recent proposal for an 18 percent tax on non-diet soda and sugary beverages containing less than 70 percent real fruit juice.



Paterson's plan is the highest tax ever proposed on food, and the estimated \$404 million in revenue it could generate in its first year would fund public health programs, including obesity prevention. If the proposal survives a comprehensive legislative and public review of Paterson's budget, it could be adopted as early as April.

"It's a whole new kettle of fish right now," said Brownell, professor of psychology and epidemiology, and director of the Rudd Center for Food Policy and Obesity at Yale. He cited the troubled economy, mounting research linking soft drink intake to health issues and a growing concern about child obesity. "I think the social situation has changed enough that these taxes are going to happen at some point. Once the door opens, I would expect there will be a flood of others wanting to go through it."

The tide may be turning already. While many New Yorkers and representatives of the beverage industry are highly critical of Paterson's tax, Brownell has had calls from advocates in two other states that he said may soon go public with similar proposals.

Over the years, the "fat tax" has also surfaced as a "snack tax," a "Twinkie tax" and a "miracle tax diet," but rarely has it gotten off the legislative floor. California, Maine and Maryland all passed taxes of about 4 to 5 percent, and all later repealed them, mostly in response to food industry resistance. Smaller taxes on junk food in more than a dozen other states have been too insignificant to drive down consumption or spark a fight with the food industry, Brownell said.

New York's proposed soda tax is exactly the kind of food tax Brownell



Kelly Brownell

favors, because the potential revenue would be dedicated to health-related programs, and he applauds Paterson's bold approach. "I give the governor credit for proposing a large tax and not pussyfooting around. It makes sense to tackle this aggressively," he said.

More than any other food category, sugared beverages have been linked to poor diet, a higher rate of obesity and increased risk of diabetes. Studies also suggest that an 18 percent increase in price would drive consumption down by about 15 to 18 percent. "If consumption of sugared beverages goes down, that could have a whopping effect on public health," Brownell said.

—Kathy Katella

Online: Yale Netcasts Kelly Brownell: Human Food Cravings

Internal medicine continues outreach with focus on "human infrastructure" abroad

For nearly three decades, the School of Medicine's international health program has provided career-changing experiences for medical residents by sending them to developing countries. Now Yale is taking the Yale/Johnson & Johnson Physician Scholars in International Health Program a step further by developing "human infrastructure" at partner sites.

Rather than helping only American doctors develop a sense of global citizenship and commitment to caring for the poor, the program has made ambitious plans to build the long-term capabilities of its sites abroad. The program, which typically sent American doctors to as many as 15 foreign sites, now focuses on only six. A sense that Western institutions had profited asymmetrically from a brain drain from developing countries—a realization prompted in part by increased international communication among researchers in the AIDS era drove the change.

"It became clear that we as faculty and Yale as an institution have an obligation ... to people all over the world," said Asghar Rastegar, M.D., new director of the international health program, which has partnered with Johnson & Johnson since 2001. Based in part on Rastegar's own experience as a faculty member at Shiraz University in Iran, the redesign emphasizes bilateral benefits and long-term in-depth commitment. Physicians in the program now serve in the host country as both learners and teachers; and they bring equipment and materials with them, helping the site itself expand its capacity to care for the sick. In turn, the host countries send physicians on learning trips to the United States.

The pilot program, developed by Majid Sadigh, M.D., associate professor of medicine, is in Kampala, Uganda, at Mulago Hospital, the teaching hospital of Makerere University. The hospital has a ward staffed full time by Yale faculty and residents working side by side with their colleagues from Makerere, and sends physicians to New Haven for specialty training. Fred Okuku, M.D., a resident physician, spent six months at Yale learning to perform mammograms and ultrasounds, then





Asghar Rastegar

returned to Uganda with the training and equipment—a mobile mammography van—to diagnose early-stage breast cancer. The inexpensive cancer treatment available at Mulago—surgery will save lives that would otherwise have been lost to a late diagnosis.

Though the program has slimmed from 15 sites to just six, those six—in Eritrea, Honduras, South Africa, Uganda, Liberia and Indonesia-are being transformed by the new philosophy. At Tugela Ferry, South Africa, a site directed by Gerald H. Friedland, м.р., professor of medicine, and devoted to research on and care of patients with HIV and tuberculosis, the husband-andwife team of Scott Heysell, м.D., м.Р.Н., and Tanya Thomas, м.р., is spending a year at the local hospital. In war-ravaged Liberia, Yale has joined five American medical schools in a collaboration with the John F. Kennedy Medical Center. And Rastegar is working with Eritrea's first medical school to develop an internal medicine residency there.

The international health program outreach continues to expand, sponsoring classes in international medicine for medical, nursing and physician associate students interested in global health. These projects, said Michele Barry, M.D., HS '77, a longtime co-director of the program who stepped down in March to become senior associate dean for global health at Stanford University, will bring fresh hope to caregivers in the sites' lowresource communities. "I think there is a role for us to really stop the brain drain-to stop people like Fred Okuku from thinking he only has a hospice," Barry said.

—Jenny Blair

Recommendations for rest periods for residents meets with skepticism

For decades, doctors in training have endured long hours and sleepless nights during residency. Due to concerns that their resultant fatigue might harm patients, in 2003 an 80-hour limit on weekly duty hours, along with a 30-hour limit on work periods, became mandatory for hospitals approved by the Accreditation Council for Graduate Medical Education. But a recent report by the Institute of Medicine (IOM) recommends stricter duty-hours rules that would allow residents more rest, while calling for stronger enforcement of existing rules.

Issued in December, the IOM report is the work of a committee of physicians and sleep experts that examined studies on the relationships among duty hours, sleep physiology and patient safety, including some research done since the 2003 changes. The committee concluded that the evidence was "nascent ... but sufficient to recommend action now." It proposed, among other changes, that residents working 30-hour periods pause on or before the 16th hour for five hours' rest, and that they be granted an uninterrupted 48 hours each month to catch up on sleep. The 80-hour weekly maximum would remain in effect, as would such other 2003 rules as 10 hours off after a work day.

Yale educators, however, have reservations about the report. Peter N. Herbert, M.D. '67, HS '69, senior vice president of medical affairs at Yale-New Haven Hospital, called it "disappointing," citing the scarcity of evidence that scheduling of duty hours affects patient safety. "It reflected, to many of us, a confusion about what their purpose was," Herbert said. "It would probably be much more worthwhile to look at what work hours and schedules do to resident education."

"We're certainly philosophically on board with believing that rested, clearthinking people provide better care," said Stephen J. Huot, PH.D. '81, M.D. '85, HS '87, chair of the primary care internal medicine residency. But, he said, these well-intended changes might actually jeopardize patients, since they would require more frequent handoffs of patient care and might diminish access to care at some medical centers.

Academic neurosurgeons greeted the report with dismay. Neurosurgical operations last longer than other types of surgery, said Dennis D. Spencer, м.р., нs '77, chair of the department, requiring longer and more flexible duty hours. "The 16-hour shift with the 10-hour-at-home rule means that our chief residents will never be able to come back to the hospital and see patients they may have operated on, or they will be unable to come to the hospital the next day," Spencer said. "They will never learn responsibility for their patients and they will erode the mentor/ student bond with attending faculty who are attempting to give them more responsibility. This destroys one of the main competencies we are supposed to be teaching-professionalism."

Though the IOM committee estimated that the cost of adopting its recommendations could reach \$1.7 billion annually, it recommended that these changes be adopted within two years.

Whether or not the new rules are adopted, the culture change alone implied by a 16-hour work period—a move toward shift work—has some physicians worried. Continuity of care and teaching a physician to "own" a patient, said Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, are valuable lessons. "This focus on work hours has removed that culture from medicine," he said. "Nobody seems to be concerned about where we're headed with this loss in continuity of care."

"We need to figure out how to continue to instill a sense of complete responsibility for the care of your patient—putting the patient's needs above your own needs and do so in an educational system that allows you to still function as a person," said Huot.

-J.B.

et cetera

MEDICAL CAMPUS GETS GREEN AWARD

The Amistad Street Building has received a gold "greenness" rating from the U.S. Green Building Council's Leadership in Energy and Environmental Design program. Among the "green" features is a 7,500-gallon tank that recycles storm water collected from the roof. Additional features include laboratory cabinetry made from wood produced in sustainable forests, a heat recovery system and energy-efficient bulbs and occupancy sensors that help cut electricity use. Recycling of renovation debris reduced construction waste by 70 percent.

The project, which provides laboratory space for the Interdepartmental Program in Vascular Biology and Therapeutics, the Yale Stem Cell Center and the Human and Translational Immunology Program, was built around the existing shell and core of the building.

"This project presented all the challenges one typically finds when striving to build sustainably in an existing building," said Virginia Chapman, director of construction and renovation for the School of Medicine's facilities office. "But we made it work—and work rather well."

—Charles Gershman

ECONOMIC SITUATION WORSENS FOR YALE

In an e-mail to the Yale community in February, President Richard C. Levin said the deteriorating economic situation would require budget cuts beyond those he had called for in December. "The mounting evidence suggesting a prolonged recession has caused us to recognize that we need to take a more aggressive approach to budget reductions for the coming fiscal year," Levin wrote.

Levin called for cuts in all 2009-2010 budgets by an amount equal to 7.5 percent of the salaries and benefits of all non-faculty staff and a 7.5 percent reduction in non-salary expenditures, up from the 5 percent he had called for in December. These measures could save \$37 million in next year's operating budget, Levin said. But, he added, "... if external con-ditions deteriorate significantly, we may be required to take further action next year."

-John Curtis

Pediatric AIDS clinic reports success

Drug protocols and other measures prevent HIV-positive births in New Haven for more than 12 years.

Born HIV-positive, for 20 years "John" relied on the Yale Pediatric AIDS Clinic to keep him healthy. That meant visits every three months and treatment that was literally hard to swallow. But John says he "loved every minute" of his time at the clinic because he could rely on the staff, even when the problem was not medical. For example, the clinic helped him find housing as a teen when his mother left the state.

Now a junior at Southern Connecticut State University, he is making plans for graduate school. He calls to let everyone



Pediatrician Warren Andiman has been treating children with AIDS since the earliest days of the epidemic. Thanks to a protocol he has established, not a single baby has been born HIV-positive in New Haven in more than 12 years. at the clinic know what's going on in his life, but he gets his HIV care at an adult clinic, where he is likely to visit three times a year. Increasingly sophisticated blood testing lets doctors fine-tune his medications to prevent resistance to antiretrovirals.

As patients like John transition into adult care, few new cases replace them. No woman known to be HIV-positive has passed on the virus to her baby in New Haven since 1996. The protocols for preventing mother-to-child transmission are so effective that the only HIV-positive infants delivered in the city over the past 13 years were born to mothers who had not been not diagnosed themselves.

"We have literally been putting ourselves out of work," said Warren A. Andiman, M.D., FW '76, professor of pediatrics and epidemiology and public health, and medical director of the Pediatric AIDS Program. An infectious disease specialist, Andiman began caring for HIV-positive infants in 1982. In the first few years, his young patients died protracted and miserable deaths, often by age 6. "There's no way to describe what it was like," he said.

Today mother-to-child transmission is a rarity in the developed world. Nationwide, the rate is less than 2 percent, which Andiman attributes to "will and money."

Widespread HIV testing allows doctors to identify women who may pass the virus on to their babies. Any HIV-positive pregnant woman in the area gets referred to Yale's High-Risk Maternity Program or a parallel program at the Hospital of St. Raphael, both of which work closely with the Pediatric AIDS Program. Such measures as giving mothers antiretrovirals during the pregnancy and administering AZT to mothers during labor and to newborns have proven successful, along with, in certain circumstances, performing caesarean sections and discouraging breast feeding.

Connecticut mandates that every pregnant woman be offered HIV testing twice. She can be offered testing again during labor. If she refuses, a newborn can be tested over her objections. In practice, almost all the mothers welcome testing.

During an HIV-positive woman's pregnancy, older children or sex partners may be diagnosed and get treatment. The woman will be connected with the adult AIDS clinic and social workers will address a wide range of practical and emotional issues. "It's a sort of seminal period, a moment when all kinds of worthwhile stuff can happen," said Andiman.

So much good stuff has happened at the Pediatric AIDS Clinic that Andiman expects it to close in the next couple of years. The few remaining patients can be transitioned to the Pediatric Infectious Disease Clinic. "AIDS is an infectious disease just like many other infectious diseases," Andiman said.

—Colleen Shaddox

A revitalized trauma section increases staff and improves care in emergency cases

On February 16, 2007, Quinnipiac University senior Benjamin Shapiro was driving down a secondary road in Hamden, Conn., at about 1 a.m. when his car slid across four lanes of traffic, crashed through a chain-link fence, flipped over a concrete barrier, slid down an embankment and landed in the Mill River. He spent the next 20 minutes submerged in icy water.

"When they pulled him out of the water there was no heartbeat, no pulse, nothing," said Shapiro's stepmother, Joan Abrams. Shapiro had suffered a brain injury, the bones in the left side of his face were crushed and his left eyeball was hanging by a tendon. Doctors put his chances of survival at well below 10 percent.

The Department of Surgery's Section of Trauma, Surgical Critical Care and Surgical Emergencies, which was recently revamped under the direction of Kimberly A. Davis, M.D., was prepared to deal with an emergency of this magnitude.

"Everyone who is a full-time member of this section is board-certified or eligible in both general surgery and surgical critical care," said Davis, who took over as section chief in June 2006. "With attending-level surgeons in the hospital at all times, we can take care of anything that comes our way, 24/7." This also means faster evaluation and response times and improved communications between caregivers as well as with family members.

"With Kim's appointment, our Level 1 trauma center has become a comprehensive acute care service, where physicians are able to function in all three areas: urgent general surgery, critical care and trauma, and that has made a huge difference in our service to the community," said Tucker Leary, vice president of administration at the hospital.

Under Davis, the number of surgeons has nearly doubled, to seven full-time surgeons providing trauma, critical care and emergency surgery. Davis is planning to fill an eighth position soon. She also initiated a weekly meeting to review cases and discuss what worked and what might have been handled differently.

And the investment is paying off. The year before Davis' arrival, the section evaluated 2,550 patients and admitted 1,650. In 2007-2008, 3,800 trauma patients were evaluated and 2,400 were admitted. The survival rate of trauma center patients is 95.6 percent, above the national average of 94 percent.

One of those survivors is Shapiro, who spent nine days in a medically induced coma, followed by surgery to rebuild his face and save his eye. He was able to return to Quinnipiac as a full-time student and graduated with his class that May.

"I look back on the day of my accident and as horrible as it was, I view it as the single best day of my life," he said. "Now, whenever someone says to me, 'How are you doing?' I can always say, 'Great.' "

—Jennifer Kaylin



A newly revamped trauma section has seen a doubling of the number of surgeons who provide trauma, critical care and emergency surgery and an increase in the number of patients evaluated and admitted.

el celeia ...

LOST IN TRANSLATION

Even as the number of Americans with limited English-language proficiency has continued to grow, many physicians try to get by with their own limited foreign-language skills or by relying on a patient's friend or family member, according to research conducted in part by the School of Public Health.

The study, published online in the Journal of General Internal Medicine in December, found that increasing the use of interpreters by hospital physicians will require "substantial" changes in hospital practice. "Residents found it difficult to change their practice, despite misgivings about the quality of care provided," said Lisa Diamond, M.D., M.P.H., a Robert Wood Johnson Foundation Clinical Scholar and lead author of the study, who is now at the Palo Alto Medical Foundation Research Institute in California. Research has shown that language barriers can lead to decreased access to preventive services, poor understanding of instructions for medications, longer hospital stays and an increased risk of medical errors and misdiagnoses.

—John Curtis

ELDERLY WANT SAY IN TREATMENT

Elderly patients with multiple medical conditions want to be involved in their treatment decisions, Yale researchers reported in the Journal of the American Geriatrics Society in October.

About 65 percent of older Medicare beneficiaries have at least two chronic conditions, and 24 percent have four or more. These patients face what are called "competing outcomes"--complex choices presented when the treatment for one condition could worsen another. Medicine for elevated cholesterol, for example, may cause leg cramps that prevent a patient from doing exercises that reduce arthritis symptoms.

Study author Terri R. Fried, M.D., associate professor of medicine (geriatrics), and her team conducted 13 focus groups with 66 people age 65 and older who had an average of five chronic conditions and took an average of seven medications. When faced with competing outcomes, Fried said, "They chose the treatment option that would maximize the likelihood of their most desired outcome."

—Ј.С.

10

A molecule that puts the brakes on appetite

Yale scientists find a family of phospholipids that curb the desire to eat in rats and mice.

That heaping pile of golden crisp French fries looks delectable, but polishing off the plate may be a tall order. New research from Yale scientists suggests that a family of phospholipids tells the brain when an animal has had its fill of fat—findings that help explain the physiologic mechanism that wards off a deep-fried feeding frenzy. And these phospholipids, called N-acylphosphatidylethanolamines, or NAPES, may hold the key to new treatments for obesity.

The human body has several builtin systems that keep us from stuffing ourselves silly. Leptin, for example, tells the brain to put the brakes on eating when fat stores are abundant. Now a team led by Gerald I. Shulman, M.D., PH.D., the George R. Cowgill Professor of Physiological Chemistry, professor of medicine and of cellular and molecular physiology and a Howard Hughes Medical Institute investigator, has identified a new class of appetite-suppressing molecules—the NAPES—that become synthesized in rats after a high-fat meal, as reported in November in the journal *Cell*.

The researchers teased apart the function of NAPES by synthesizing the most physiologically abundant NAPE and injecting it into rodents. They found that the higher the concentration of the phospholipid, the less the rodents ate. Furthermore, like someone sitting back after a feast, the NAPE-injected mice

lounged about and groomed themselves even though they ate only a mini-meal.

Shulman's group discovered that NAPES, like certain other chemicals that help to control appetite, exert their effects via the central nervous system. They appear to be synthesized in the small intestine after a high-fat meal but they then get dumped into the blood and lymphatic system, putting them on a fast track to the brain. When Shulman's team injected nanomolar amounts of NAPE directly into rodent brains, it slashed the animals' appetites by more than 50 percent and shut down the activity of NPY neurons, which stimulate appetite.

On a roll, the researchers decided to treat the rats with NAPE for five straight days. They found that the rodents ate 30 percent less food and shed a significant amount of weight.

The race is now on to see whether these rodent findings translate to humans. Shulman's team is investigating NAPE regulation in humans following feeding, and the researchers soon plan to treat monkeys with NAPES to observe the effects on appetite. Provided those studies pan out, Shulman is eager to see whether NAPES can reduce food intake in humans. If they do, NAPES could serve as the basis of novel appetite-suppressant or obesity-fighting drugs. "Obesity is a major health problem, and we have very few treatments available," Shulman said. "We are always looking to better understand appetite regulation, and NAPES may be a new physiological regulator of appetite."

—Kara A. Nyberg

"Dry cleaning" effect—research shows how mice, and people, work on autopilot

By watching mice navigate a customdesigned swimming pool. Christopher Pittenger, M.D., PH.D., assistant professor of psychiatry, has discovered an ongoing competition between one part of the brain devoted to active seeking and another part devoted to mindless cruising. These two sections of the brain, his research shows, can inhibit each other, depending on the task at hand or, in this case, at paw. The competition, which likely occurs in people as well, may explain why it can be so hard to alter set routines, and could explain the power of such unwanted habits as drug addiction or obsessivecompulsive behaviors.

Pittenger's study found that two parallel learning and memory systems that reside in different parts of the brain can block each other's functions. The striatum powers up when—as if on autopilot-we embark on a wellknown route like driving to work. The hippocampus comes into play when we need to think about where we're going, as when we're looking for a new address or detouring for an errand. The study found that when one system is impaired, the other is enhanced: in mice, injuring the striatum made the animals worse at locating a visual target in a water maze, but better at more active hippocampus-based navigational skills, and vice versa.

This reciprocal inhibition may explain the difficulty many people have in breaking from an entrenched routine. "This is why I cannot, for the life of me, remember to drop off my dry cleaning on the way to work," said Pittenger, whose findings were published in October in *Proceedings of the National Academy of Sciences*.

"When you have driven the same route many times and are doing it on autopilot, it can be really difficult to change. If I'm not paying enough attention right at that moment, if I am thinking about something else, I just sail right on by."

On a more serious note, the findings may also help explain the behavioral peculiarities seen with some brain diseases. Alzheimer disease, for example, destroys hippocampal function. That may be why many people with this disease fall back on old behaviors, like repeatedly returning to a previous address, thinking it is still home. Other diseases, including obsessive-compulsive disorder (OCD) and Parkinson disease. involve striatal malfunction. Pittenger's new results emphasize that this striatal malfunction is likely to lead to changes in the function of the hippocampus, too, which may either compensate for or exacerbate the symptoms of the disease.

Understanding the connections between memory systems may offer new ways to treat serious behavioral problems. "A lot of psychiatric diseases are characterized by recurrent, maladaptive patterns of thought or behavior," says Pittenger, who is also director of the Yale Obsessive-Compulsive Disorder Research Clinic. "People with oCD or drug addiction just keep doing the same thing and can't seem to stop, no matter how hard they try."

Treatment for OCD often includes cognitive behavioral therapy, which works by engaging a more reflective thinking mode to try to control automatic behaviors. Pittenger speculates that the process may work by recruiting one brain region to overcome an excess in the other. If so, it might be possible to develop drugs to make cognitive therapy more effective by enhancing or balancing the activities of the striatum or hippocampus.

It's quite a leap from mice paddling in a pool to human disease, Pittenger said, but learning how basic normal memory systems work in animals is an important first step.

—Pat McCaffrey

et cetera

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BIOMARKER FOR LUNG CANCER RISK

A genetic variation could explain why some people have a greater risk of developing lung cancer, Yale scientists reported in the journal *Cancer Research* in October.

"Only 10 percent of smokers will develop lung cancer in their lifetime, and genetic testing to determine the population of smokers who are most predisposed to develop the disease is needed to help guide better evaluation for these people," said Joanne B. Weidhaas, M.D., PH.D., assistant professor of therapeutic radiology at Yale. She was senior author of the study, in collaboration with Frank Slack, PH.D., associate professor of molecular, cellular and developmental biology.

"We looked for the effects of genetic variations within a human oncogene known to be affected by tiny RNA molecules called micro-RNAs," said Slack, explaining their discovery of the biomarker. These variations, called single nucleotide polymorphisms, predicted a significant increase in non-small-cell lung cancer risk in people with a moderate smoking history as well as in nonsmokers.

—John Curtis

YALE PAPER AMONG BEST OF 2008

An article by Yale scientists on the formation of cell membranes has been named one of the top scientific papers of 2008 by the journal *Nature*.

The paper, published in *Cell* in March 2008, explored how cells shape their membranes into tubes, spheres and other curved structures that they need in order to move, communicate and reproduce. Scientists including Vinzenz M. Unger, PH.D., associate professor of molecular biophysics and biochemistry, M.D./PH.D. student Adam Frost and Pietro De Camilli, M.D., the Eugene Higgins Professor of Cell Biology and Neurobiology, established how banana-shaped proteins called F-BAR domains form curved scaffolds that allow cell membranes to assume those forms.

Using a combination of cryoelectron microscopy and cell biology experiments, the team found that F-BARs accumulate side by side on flat membranes until attractive forces cause them to turn onto their tips en masse and pull the now-curved membrane into shape.

-Peter Farley

12

Uncovering the toxins in our daily lives

A new book by a lecturer in public health describes what's safe and what's not in household products.

Toxicologist Gary Ginsberg, PH.D., has good news about the environmental contaminants we encounter in our daily lives. "One of the major myths is that the environment is worse than it's ever been," said Ginsberg, the senior toxicologist at the Connecticut Department of Public Health and a lecturer at the Yale School of Public Health. "As a matter of fact, a lot of things are better now than they ever were."

For instance, pesticides used in farming are less hazardous and less persistent than the banned chemicals of the 1950s, 1960s and 1970s. Paint and gasoline no longer contain lead. Asbestos has been phased out of building materials, and intact asbestos can be safely left in place. And although a staggering number of people are worried about mold in homes and schools, Ginsberg said that humans have lived with mold for millennia, and the fungus is unlikely to cause lung damage. "It's a crop you don't want to grow in your house, but it's something you shouldn't freak out about."

Still, research and reporting regularly bring to light serious risks from toxic chemicals, said Ginsberg, "and the headlines don't answer the specifics of your situation." To help the public distinguish between major and minor risks, Ginsberg collaborated with health department colleague Brian Toal, M.S.P.H., to write a guide, *What's Toxic, What's Not*, published in 2006.

"Rather than answer questions one phone call at a time, we decided we would try to put it all together in a somewhat encyclopedic but accessible way," said Ginsberg. He and Toal considered a range of potential hazards: hormones in hamburgers, carcinogens in bubble bath, toxic fumes from overheated Teflon and volatile chemicals in toilet cleansers and drain uncloggers. (Ginsberg said that using harsh cleaners is "like using the atom bomb to clean the bathroom." He recommends hot water and detergent instead.) The authors discuss power lines, toxic waste dumps and cancer clusters.

Ginsberg cites the top five risks Americans face as radon gas, indoor air pollution, mercury in fish, lead paint and carbon monoxide. The book advises readers to test for carcinogenic radon gas at home and to vent appliances and woodstoves properly, to burn only dry hardwoods and to clean chimneys regularly. Because most fish contain mercury, the book suggests no



Gary Ginsberg is the co-author of What's Toxic, What's Not, an accessible guide to the risks of common household products.

more than two fish meals per week, with only one containing farmed fish. People living in houses more than 30 years old should watch for chipping paint, especially on windowsills. Occupants of houses built before 1987 should test their drinking water for lead, and all children should get blood tests for lead at ages 1 and 2.

Ginsberg himself buys such products as dish soap and shampoo at the health food store rather than the supermarket. Dangers in supermarket items include volatile organic compounds in cleaning products as well as reproductive toxins and carcinogens in cosmetics. "There's no gatekeeper at the supermarket, and the Consumer Product Safety Commission doesn't regulate these things," Ginsberg said.

With each new headline in the media, Ginsberg gets new questions. For example, consumers have begun worrying about plastic baby bottles and water bottles containing Bisphenol A (BPA), a chemical used since the 1950s to make polycarbonate plastics that was developed in the 1930s as a synthetic estrogen. Recent animal studies have shown that BPA can disrupt the endocrine system. The Canadian government announced in October 2008 that it is banning polycarbonate baby bottles containing BPA. To provide information about such emerging issues, Ginsberg has established a website: whatstoxic.org. He also hosts a radio show, *Greener Living with 'Dr. G*,' which can be heard (locally or on the Internet) on WTIC-AM, Saturdays from 4 to 6 p.m.

—Cathy Shufro

Bookshelf focuses on books and authors affiliated with the School of Medicine. Send suggestions to Cathy Shufro at cathy.shufro@yale.edu.

BOOK NOTES



High Risk Obstetrics: The Requisites in Obstetrics and Gynecology

by Edmund F. Funai, M.D., associate professor of obstetrics, gynecology and reproductive sciences. Mark Evans, M.D., and Charles J. Lockwood, M.D., chair and the Anita O'Keefe Young Professor of Obstetrics, Gynecology and Reproductive Sciences (Elsevier) This volume offers guidance for assessing and managing high-risk pregnancies. The book includes tables that present differential diagnoses and recommendations on lab values and treatments. Case studies and illustrations accompany coverage of antepartum care, medical complications of pregnancy, fetal disorders, fetal surveillance, intrapartum complications and puerperal disorders.

Stoelting's Anesthesia and Co-Existing Disease, 5th ed.

by Roberta L. Hines, M.D., HS '77, chair and the Nicholas M. Greene Professor of Anesthesiology, and Katherine E. Marschall, M.D., assistant professor of anesthesiology (Elsevier) This edition has been updated to reflect the latest information to help clinicians avoid or manage complications stemming from pre-existing medical conditions. Organized by disease, the new edition provides guidance on definition, current pathophysiology and pre-, intraand postoperative factors of the disease process, anesthetic judgment and management. It provides case studies that exemplify how to overcome a wide range of challenges, and it examines specific anesthesia considerations for special populations, including pediatric and geriatric patients.

Motion Preservation Surgery of the Spine: Advanced Techniques and Controversies

by James J. Yue, M.D., associate professor of orthopaedics and rehabilitation, Rudolph Bertagnoli, м.D., Paul C. McAfee, м.D., and Howard S. An, M.D. (Elsevier) This book provides an introduction to motion preservation surgery and discusses surgical considerations and cervical total disc arthroplasty. The text examines the advantages and disadvantages of the full range of nonfusion technologies and presents stepby-step, illustrated operative guides to achieve optimal outcomes. The book is accompanied by a DVD featuring three hours of surgical video.

Dermatopathology: Diagnosis by First Impression

by Christine J. Ko, M.D., assistant professor of dermatology and pathology, and Ronald J. Barr, M.D. (Wiley-Blackwell) This guide introduces a simple and effective way to approach a slide and focuses on a selection of commonly tested entities, showing low- to high-power views. Major differences among diagnoses that are sometimes confused are emphasized on "Key Differences" pages. The book contains minimal text and should be used as a companion to dermatopathology textbooks and as a pictorial reference and study tool.

The Uncertain Art: Thoughts on a Life in Medicine

by Sherwin B. Nuland. м.р., clinical professor of surgery (gastroenterology) (Random House) This volume is a collection of essays about the mix of expertise, intuition, sound judgment and chance that plays a part in a doctor's practice and life. Drawing from history and his own experiences, Nuland includes topics ranging from the primitive procedures doctors once practiced with good intentions—such as grave robbing and prescribing cocaine as an anesthetic—to gene therapy, the adoption of Eastern practices like acupuncture and the complex moral and ethical guandaries confronting healers that arise from such innovations as cloning.

Trauma-Centered Group Psychotherapy for Women: A Clinician's Manual

by Hadar Lubin, M.D., assistant clinical professor of psychiatry, and David R. Johnson, PH.D., associate clinical professor of psychiatry (Routledge) This manual is a theory-based, field-tested model of group therapy for traumatized women. It includes clinical examples, a session-bysession guide for clinicians and a workbook for clients. Topics include managing traumatic re-enactments, a developmental theory of trauma and posttraumatic stress disorder and guidance in handling difficult treatment and clinical situations. The authors also discuss the use of testimonials and ceremonial structures to heighten the therapeutic impact.

The Marshall Plan: Lessons Learned for the 21st Century

edited by Eliot Sorel, M.D., FW '75, and Pier Carlo Padoan, M.D. (OECD Publishing) This book examines the historical, diplomatic, economic and strategic aspects of the European Recovery Program—popularly known as the Marshall Plan—that brought Europe out of the chaos, hunger, poverty and desperation of World War II. Contributors address 21st-century applications of lessons learned from the Marshall Plan.

Essential Otolaryngology: Head and Neck Surgery, 9th ed.

by K. J. Lee, M.D., associate clinical professor of surgery (otolaryngology) (McGraw-Hill) This otolaryngology primer delivers the latest critical information to help treat conditions involving the head and neck, such as sinusitis, sensory disorders, cancer and sleep disorders. This edition contains new chapters on cysts and tumors of the jaw, TNM classification in otolaryngology, head and neck surgery, and malignant melanoma.


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Non-Invasive Management of Gynecologic Disorders

edited by Aydin Arici, м.р. '50, professor of obstetrics, gynecology and reproductive sciences, and Emre U. Seli, м.D., assistant professor of obstetrics, gynecology and reproductive sciences (Informa Healthcare) This text provides information on currently available options for gynecologic disorders suitable for nonsurgical management. It offers guidance to physicians on how and when to choose more conservative modalities and how to differentiate between the variety of treatment options available. The authors take an evidence-based approach to topics including management of ectopic pregnancy, pregnancy loss and termination, infertility, chronic pelvic pain, endometriosis and dysfunctional uterine bleeding.

How to Think Like a Radiologist: Ordering Imaging Studies

by Tara Marie Catanzano, M.D., assistant professor of diagnostic radiology (Cambridge University Press) This pocket guide provides guidance in choosing which type of imaging study best answers the clinical question posed. The book addresses imaging studies by modality, body region and type of study in bulleted outline format. It discusses general considerations for each modality—including advantages and disadvantages—as well as patient preparation and requirements for each type of examination.

The Nursing Home Guide: A Doctor Reveals What You Need to Know About Long-Term Care by Joshua D. Schor, M.D. '85

(Berkley/Penguin) The author guides the reader step by step through the process of placing a loved one in a nursing home or long-term care facility. He covers such topics as questions to ask about medications, meals and activities; deciding whether assisted living may be a viable alternative; determining whether a family member needs long-term or subacute care; and knowing your rights and getting the information you need.

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

IN CIRCULATION

Library initiative links Third World doctors and researchers to journals

Just seven years ago, clinicians and scientists in the developing world could get hold of—on average—only two international medical journals, according to the World Health Organization (WHO). And in the poorest countries, fewer than half of the doctors and researchers could put their hands on a single journal.

Now, through a WHO program called HINARI, they have electronic access to 6,000. The program makes journals and databases available to health care professionals in 3,600 hospitals, medical schools and other institutions in 108 countries from Afghanistan to Zimbabwe. Subscription rates range from nothing in the poorest countries to \$1,000 annually per institution in more affluent countries.

Yale librarians including Kimberly Parker, M.I.L.S., have played crucial roles in developing HINARI. Parker headed the electronics collection for Yale's library system when the project was conceived in 2001; researchers from resource-poor countries had told wHO officials that without access to biomedical information they could not be members of the international research community. Within months, several major publishers had agreed to donate access to their journals, and HINARI was launched in January 2002. Last spring Parker took over as program manager of HINARI in Geneva.

Yale librarians continue to contribute. When a researcher in Ecuador peruses a journal, or a gynecologist in Vietnam reads about screening for anemia, each depends upon the support of Yale librarian Daniel Dollar, M.L.S., and his staff, who make sure that links work and add journals and databases to the everexpanding system. "They actually have access to more journals than we do," said Dollar.

Because of HINARI, Parker said, more scientists "are contributing to the global conversation in important ways, often on topics the rest of us are ignoring."

Senegalese urologist Mohamed Jalloh, M.D., depends on HINARI to search the medical literature and find such clinical information as drug dosages. Just three years out of residency, Jalloh says he has had 13 articles published. "It is very important for us to have access to good-quality peer-reviewed publications," he said.

-Cathy Shufro

In Circulation focuses on activities at the Cushing/Whitney Medical Library. Send suggestions to Cathy Shufro at cathy.shufro@yale.edu.



LTAUX IVEN

Connecticut lags in long-term care for elderly and disabled

Connecticut has made inroads into shifting long-term care for the elderly and people with disabilities from institutions to community-based programs, but according to a Yale researcher it lags behind many other states. "Connecticut is making important progress, but there's a long way to go," said Leslie Curry, PH.D., M.P.H., a research scientist at the School of Public Health who spoke at a session in the Aging Research Seminar Series in February.

Spurred by a 1999 U.S. Supreme Court ruling, states have begun to shift long-term care from nursing homes to community-based options, largely because nursing home care is about twice as costly as community-based care and because people prefer community settings. With \$56 million in federal grants, Connecticut has increased the proportion of Medicaid clients receiving community-based care from 46 percent in 2002 to 51 percent in 2006, Curry said.

Nationally, though, Connecticut "is not a leader," and Curry said the state needs to streamline its organization, increase community-based options and enhance consumer-directed models of care in order to reach its goal of having 75 percent of Medicaid recipients who need long-term care in communitybased settings by 2025.

—John Dillon



Zimbabwe cholera outbreak has roots in corruption

When cholera struck Zimbabwe last summer, international aid poured into the African country. Despite those resources, however, fatalities increased among those infected. "One in 20 people was dving, and 80 percent of those deaths were preventable." said Chris Beyrer, M.D., M.P.H., professor of epidemiology at the Johns Hopkins Bloomberg School of Public Health, at a talk at the School of Public Health in February. Beyrer investigated the health care system in Zimbabwe last year on behalf of Physicians for Human Rights.

The reasons for the epidemic and its high mortality rates, Beyrer said, stem from the corruption of President Robert Mugabe's administration, which enriched itself at the public's expense. "I have never seen a health care system collapse so extreme," Beyrer said. Public hospitals and clinics shut their doors, and for political reasons, the government had handed over public water supplies to cronies. As a result, untreated sewage flowed into reservoirs of drinking water.

"If you want to create a cholera epidemic, this is the way to do it," Beyrer said. "It is very hard to imagine a public health solution to these problems without addressing the politics." ---John Curtis Physicians must know how to blow the whistle on torture

Physician complicity in torture at Guantánamo and Abu Ghraib reveals a serious gap in medical education, said former Yale professor Barbara Burtness, M.D., now chief of head and neck medical oncology at Philadelphia's Fox Chase Cancer Center.

Speaking at the Program for Humanities in Medicine in January, Burtness said that physicians and other health care providers had abetted such tortures as waterboarding, granted medical clearance for harsh interrogations, permitted forced feeding, offered privileged information on prisoners' phobias, withheld care and falsified death certificates. In Iraq, she said, "they medically approved biopsychosocial interrogation plans."

"I wondered," said Burtness, "Were they people I had gone to medical school with, or people I had trained?"

Medical students, she said. should learn standards for treatment of prisoners and understand such ethical codes as the Declaration of Tokyo. which addresses torture. They should recognize signs of torture and understand that, if they participate in abuse, they could be accused of war crimes. Physicians should also know how to blow the whistle: just as they carry notes on how to measure blood gases, she said, they should carry phone numbers for reporting torture.

—Cathy Shufro



Parental consent needed for genetic screening

Most of the 4.3 million babies born in the United States each year are screened without parental consent for up to 50 genetic disorders that may cause such severe conditions as mental retardation. But at a pediatric grand rounds in February, Lainie Friedman Ross, M.D., PH.D. '96, the Carolyn and Matthew Bucksbaum Professor of Clinical Medical Ethics at the University of Chicago, argued for changing the recommendations governing parental consent.

"If we had parental consent for these tests it would show respect for parental autonomy in health care decisions for their children, which is required for all other health care, and it would also allow us to enroll the children in research protocols," Ross said. "That is the only way we will learn the natural history of these very rare diseases, understand who needs to be treated and develop effective treatments for them."

Ross also questioned the current policies of the American Academy of Pediatrics and the American College of Medical Genetics, which proscribe testing children for adult-onset conditions like breast cancer. Some parents want the information early for psychosocial reasons. While predictive testing should be discouraged, Ross maintained that parents, not physicians, should have the final say in testing children.

—Alix Boyle

Cautionary tales for WWII GIs

The Medical Historical Library's art collection includes graphic posters that warned soldiers and sailors of the dangers of venereal diseases.



Posters that warned enlisted men of the dangers of unprotected sex were part of a larger educational campaign to stem the spread of sexually transmitted diseases during and after World War II. The posters, which were prominently displayed at military bases, were intended as reminders that would buttress messages imparted through filmstrips and lectures. The messages took different approaches, some warning against prostitution and cautioning, as in the poster at right, that "They don't wear labels."



By Colleen Shaddox

She's no idealized oil painting. The lines around the mouth tell you she's been around the block. She might have stepped out of a dime detective novel, a wrong number who conned some farm boy into giving up his heart and his wallet. She is literally falling out of her too-tight dress. One hand rests on a cocked hip while a cigarette smolders in the other. Her hennaed hair is tightly curled. She arches a plucked brow and forms her rouged lips into a bitter pout.

"Danger Disease Ahead!" the poster warns. Just in case the message is too subtle, a large orange banner at the bottom spells it out: "Gonorrhea Syphilis." This unnamed woman was created to warn World War II servicemen about venereal disease (VD).

The Medical Historical Library's holdings include etchings by Rembrandt, portraits of the world's most eminent physicians stretching back to Hippocrates and reverent depictions of kings healing scrofula with the "royal touch." It may seem incongruous that a graphic—in both senses of the word—and cautionary portrayal of a loose woman would find a home here. For several years, however, the library has been adding to its collection of public health posters.

"What is represented in art, or fine art ... is limited," explained Susan Wheeler, curator of prints and drawings. "Moving into public health posters allowed us to represent more medical subjects in the collection."

In 2004, just as the library had made a strategic decision to acquire more posters, it received a large gift of turn-ofthe-century French advertising and public health posters from collector William H. Helfand, who has since made additional gifts. Posters were often produced in large numbers, explained Wheeler, and so copies reside in many attics and garages. As websites catering to collectors begin to spring up, owners realize that they are storing a saleable commodity, and more posters become available. The library is adding its posters to the Medical Digital Library so that they will be widely accessible.

An exhibit in the Cushing Rotunda through the winter featured a trio of posters produced by the U.S. Navy during World War II to warn sailors about sexually transmitted diseases. Some other subjects addressed in the collection include hygiene, nutrition, AIDS, tuberculosis, cancer, polio and children's health. All the posters have a common purpose: to change human behavior. So their images and language are strong and direct.

The library's selection of World War II anti-VD posters is a prime example. A sailor leans against the ship's rail with "VD" painted in huge orange letters on the back of his T-shirt. The caption reads, "Nothing to be proud of." In another poster, a sailor paints "VD" in the same bright orange across the deck of a battleship. "Don't smear your ship," the poster implores. The caution against letting down one's comrades is a recurrent theme, explained Wheeler.

The wartime military gave every serviceman training about preventing venereal disease and access to prophylactics. When men were infected, they were urged to see military doctors as soon as possible. A number of posters warned against "quacks" and home remedies. "Rapid treatment centers" gave prostitutes access to drugs to halt transmission. The anti-VD campaign was effective. By the end of the war, the infection rate among servicemen was no higher than that of the civilian population.

In April and May, the library will feature early Soviet posters, again on the theme of venereal disease. The library has acquired a complete set of posters from the Soviet campaign of 1928, so viewers can get a full picture of the messages that Russian public health officials were sending.

Colleen Shaddox is a freelance writer in Hamden, Conn.





Don't be a casualty to Venereal Disease It Can Happen to You! PROPHYLAXIS PROVIDES PROTECTION





The posters used a variety of approaches to convey their message. The one at far left called to mind family and the possibility of lost dreams. A specific concern was that after the war soldiers would bring disease home. The poster at left depicted VD as an enemy to be conquered through prevention. And the posters above, part of a series, invoked shame and guilt. Soldiers and sailors could not let their buddies down by getting sick—incapacitated servicemen could not be part of the team.





200 Years of Medicine at Yale

Cast your votes for the most significant events and personalities of the school's first two centuries.



Nearly 200 years ago, in October 1810, the Connecticut legislature passed a bill establishing the Medical Institution of Yale College, a joint venture between Yale and the Connecticut State Medical Society. The resulting institution then consisted of four professorships appointed by the Corporation of Yale College after nomination by a joint committee of the corporation and the medical society. The fledgling medical school opened its doors in 1813 with those four professors, an adjunct professor and a student body of 37. The course of studies consisted of a few months of lectures in a classroom. Only three students would graduate with medical degrees in 1814.

Next year the medical school will mark the start of its third century with a series of special events and exhibits and the publication of a book looking at the personalities and forces that shaped medicine at Yale. Yale Medicine would like readers' opinions about those influences, as well as their recollections of medical school life over the last half century or so. Was Milton C. Winternitz, M.D., the so-called "steam engine in pants" who established the Yale system of medical education, the most dynamic of all deans? Was his educational philosophy the driving force behind the school's extraordinary growth in reputation? Was Paul B. Beeson, M.D., the most exemplary clinician, or was it John P. Peters, M.D.?

We'd like to hear from you. On the following pages are 10 questions about the history of the School of Medicine and your experiences here compiled by the editors of *Yale Medicine*. Please take a moment to detach or copy these pages, check off



your favorites or nominate your write-in candidates—along with your comments and reminiscences—and return it in the envelope provided inside the back cover of this magazine. (There's also a Web version of this survey at yalemedicine.yale. edu/bestofyalemed.) There are many significant events, findings and discoveries to choose from, but we ask that you select only one response per question, or write in your nominees for the "best of the Yale School of Medicine."

So whether you feel that the neuro rotation in third year or that role in drag during the second-year show was the pinnacle of your medical school experience, take a few minutes to look back and share your memories, as well as your nominations for the medical school's best of everything. YM



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The best of two centuries

The editors of *Yale Medicine* would like your opinions on the most significant events and personalities to shape the medical school since its founding in 1810. To start the ball rolling, we've suggested a few contenders, but these are just suggestions. We hope the collective wisdom of thousands of alumni, faculty and former house officers on our mailing list will produce other candidates and sharpen our focus when it comes to describing the forces that have made Yale School of Medicine great over the years. Your votes will be counted and your comments included in a follow-up article in *Yale Medicine* in time for the school's Bicentennial celebration in 2010-2011.

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In addition to voting, please tell us the thinking behind your choice in the space provided for comments. We've also included several questions about the best aspects of Yale School of Medicine as you experienced them during your student years.

Please complete this survey online at yalemedicine.yale.edu/bestofyalemed, or fill out the questionnaire that follows and return it in the envelope provided inside the back cover of this magazine.

Contact information:

I A M E		STRE	ET AD	DRESS
- MAIL		CITY		STATE ZIP
W th	hat event in the history of Yale School of Medicine had e greatest impact in shaping the school?	2.	Wh me	at was the greatest scientific advance made at the dical school?
	Founding in 1810 Admission of women in 1916			John Peters' transformation of clinical chemistry into a discipline of precise, quantitative indicators of disease
01	Creation of the Yale system in the 1920s			Dorothy Horstmann's finding that the polio virus enters the central nervous system through the bloodstream, paving the way for the Salk vaccine
	DMMENTS		П отн	The first antiviral drug, discovered by William Prusof
			coi	MMENTS
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3.	 What was the medical school's greatest clinical advance? Discovery and successful testing of the therapeutic properties of nitrogen mustard, the first anticancer drug First successful use of penicillin in the United States Introduction of fetal heart monitoring in the 195os OTHER COMMENTS 	4.	Who among the faculty possessed the most extraordi- nary scientific mind? John Fulton Dorothy Horstmann George Palade OTHER COMMENTS
5.	Who was the greatest personality to shape the school?	6.	Who was the medical school's most outstanding clinician?
	 Milton Winternitz, dean from 1920 to 1935 Vernon Lippard, dean from 1952 to 1967 OTHER COMMENTS 		Edith Jackson Paul Beeson OTHER COMMENTS
7.	Which basic science class impressed you the most?	8.	What was your most valuable clinical experience at Yale?
э.	Which extracurricular activities were the most enjoyable?	10.	What is your favorite memory of medical school?







TOPLEFT When Dolothy Horstmann applied to Yale for a fellowship during World Warll, he interview did not go well. Francis Gillman Blake, the acting dean, told her "how the last woman he had on the house staff did something awful," she recalled. "If a woman on the house staff did not live up to expectations it was emembered for the next 50 years," she told him, "but if the person was a man, it was forgotten by the next year." Blake left the hiring decision up to John Paul, a young pathologist who had co-founded the Yale Poliomyelitis Study Unit in 1931. Ho stman, wat he open a na rave, the way of a point a char with her diaco any the her way enters the her of sign and the the bloodstration in a char shown here in her faith and the '970s, was the first woman of appointed a full mofessor to the medical school

TOP RIGHT Women cave become a ubiquitor s presence in classification clinics and laboratories over the years Sara Henry, a esearch as inciate in neurology, works in the laboratories of neurologist Jana Preiningerova who studies multiple sclerosis, MR analysis and cer-based thera ries for multiple sclerosis



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scientist built a better mouse

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How a

By inserting human system genes into mice, immunobiologist Richard Flavell and his team are creating a mouse with a working human immune system. Their goal is a system for testing vaccines and therapies against diseases that kill millions.

Story by Michael Fitzsousa Photograph by Frank Poole

PREVIOUS PAGE Richard Flavell chairs his department and oversees multiple research projects, yet he still finds time for his other passion, rock 'n roll.

In March 2006, eight healthy volunteers in London received an experimental drug that showed promise for treating rheumatoid arthritis and other autoimmune diseases. In animal tests, the drug, named TGN1412 by its developer, the German biotech company TeGenero, caused T-cells to proliferate, especially a subset known as regulatory T-cells. These cells calmed the immune system, leading TeGenero to believe its candidate molecule would ease symptoms in diseases in which the body is attacked by its own sentinels.

That was the hope. But when TGN1412 was tested in humans, disaster ensued. The six young men who received the drug (two volunteers were given a placebo) became severely ill within 90 minutes, suffering headaches, shivering, searing pain, swelling and nausea. Within 12 hours, one was on a ventilator and all six were admitted to intensive care. Then their organs—kidneys, lungs and livers—began to fail and their T-cell counts, instead of proliferating, dropped to close to zero.

What went wrong? Writing in *The New England Journal* of *Medicine* later in 2006, the intensive care team that rescued the six men reported that TGN1412 had launched a "cytokine storm"—the rapid and overwhelming release of toxic immune system molecules. Nothing in the animal studies had suggested this reaction was possible, and the human subjects had received only one-500th of the dose that had proved harmless to mice.

Although Richard A. Flavell, PH.D., was not involved in this near-fatal clinical trial, its lessons were not lost on him and on other scientists who use animal models to understand human biology and pathology. Studies in lower organisms from yeast, worms and fruit flies up the chain to nonhuman primates—are powerful precursors to research in people, says Flavell, the department chair and Sterling Professor of Immunobiology at Yale and a Howard Hughes Medical Institute (HHMI) investigator. The vast majority of genes in flies have human homologues, and the genomes of mammals and primates are closer still to our own genome. But what works in mice may not work in humans.

Human molecules in a mouse

Since the 1980s, Flavell had been engineering mice by "knocking out" specific genes or inserting them, with great effect. His group's work led to the development of a vaccine against Lyme disease and to a more detailed understanding of other disorders, including diabetes, lupus, asthma, Crohn disease and multiple sclerosis. But Flavell and his colleagues asked whether there might be a better way: "What if there was an experimental animal with a human immune system? How much easier would it be to predict what would happen?"

When the Bill and Melinda Gates Foundation announced its Grand Challenges in Global Health in 2003, with a goal of creating new vaccines for diseases in the developing world, Flavell and several of his collaborators realized that such an experimental mouse would be an invaluable tool. Their proposal was among 1,500 submitted to the Gates Foundation and one of 43 funded in the first round of grants in 2005. Flavell's group at Yale and his collaborators in Switzerland and New York received \$17 million. Their goal is to generate mice in which human immune system genes replace those of the mouse "so that they can support the development and function of human immune cells engrafted into the mice. This should permit reliable assessments of weakened live vaccines prior to human trials," according to the Gates program.

While this "human immune system mouse" builds on previous advances by other scientists, it represents a major shift in thinking. "Nothing of this kind of grand vision has been attempted before," says David G. Schatz, PH.D., a faculty colleague. Flavell's group is inserting into mice the cytokines and other molecules that immune cells use to summon other cells, the markers that establish identity and mediate transplant acceptance or rejection, and the receptors on which cells rely to recognize viruses and bacteria.

So far, Flavell's group has successfully altered or inserted nine human immune system genes into the experimental mouse. "I think we'll have a usable system in 15 months," he says.

An unusual path

When Flavell was recruited to Yale in 1988 to head the medical school's newly established Section of Immunobiology, he came with an unconventional pedigree: educated at the University of Hull in the north of England, Flavell had trained and taught at universities in Europe before leaving academia for a job in business. Scientists do that all the time. But after six years running the research division at Biogen, one of the early biotech companies that emerged in the 1980s, Flavell returned to academia. That's much less common, and often difficult to accomplish after so much time out of the funding stream that supports academic scientists.

Twenty years later, immunobiology at Yale is considered one of the top programs by its peers. It was ranked No. 1 among immunology graduate programs in the *Chronicle of Higher Education*'s 2006 Faculty Scholarly Productivity Index, which counts scholarly publications, citations, grant dollars, awards and honors in its assessment of the best departments in the United States. Flavell has authored a number of highly cited papers and has been recognized with science's top honors: he was made a member of the Royal Society in 1984 and elected to the National Academy of Sciences in 2002 and the Institute of Medicine in 2006.

Immunobiology's rise at Yale may have resulted in part because of—rather than in spite of—Flavell's unconventional approach to his career and to science. For example, he leads one of the larger university-based lab groups in the world, but while he is a scientist with significant clout, he is anything but a top-down leader. "Richard couldn't care less where a good idea comes from, as long as it's a good idea. He's very good at gathering information, building consensus and then making a decision," says Schatz, professor of immunobiology and an HHMI investigator. "It's very inclusive."

No prima donnas

This congenial atmosphere may stem from a decision Flavell and his Yale departmental co-founders—colleague Alfred Bothwell, PH.D.; former professor H. Kim Bottomly, PH.D. (now the president of Wellesley College); and Bottomly's late husband, Charles Janeway Jr., M.D.—made at the beginning. "We wanted to have outstanding people working in complementary areas using different approaches," Flavell says. "But there was one other thing that was really essential—no prima donnas. So we hired people who were outstanding but were all easy to get along with."

The department now numbers 13 primary faculty and close to 200 researchers overall, including faculty with secondary appointments as well as research scientists and postdocs. Flavell's own lab has more than 40 people working on a combination of projects funded by HHMI, the National Institutes of Health and the Gates Foundation.

Flavell has trained several dozen young scientists from around the world who rotated through his lab as postdocs. In selecting them he has looked for "a combination of creativity and the ability to get something done." Most have gone on to highly productive careers in the United States and abroad. For example, Lena Alexopoulou, PH.D., who earned her doctorate in Greece before doing her postdoc at Yale, is now a group leader at the Centre d'Immunologie de Marseille-Luminy in France. In 2001 she and Flavell published a paper in *Nature* showing for the first time that *toll*-like receptors (TLRS, molecules at the core of the innate immune response) play a role in the recognition of viruses. With more than 1,000 citations, the paper is one of the most highly referenced in the rapidly expanding TLR field.

Alexopoulou says that Flavell's mentoring launched her career and gave her an appreciation for how to manage people in her own lab. "He knows how to motivate people," she says.



For almost as long as he's been at Yale, Richard Flavell has played guitar in the "lab rock" band, the Cellmates. Colleagues and band members have included former pharmacology chair Leonard Kaczmarek on guitar, former cell biology chair Ira Mellman on bass and Flavell's wife, Madlyn, on keyboards. The Cellmates have recorded such science rock songs as "She's a Knockout" and "Molecular Millionaire."

"He gives people a chance to develop their own ideas and projects. He provides you with everything you need that he can offer you—connections, money, scientific information—and he's very open to new ideas."

As a result, says Deputy Dean Carolyn W. Slayman, PH.D., "any wonderful young postdoc ... would just die" for a slot in Flavell's lab. "He's got a terrific knack for doing translational research and training people in it. And that's led to an amplification factor—there are more scientists doing this kind of extraordinary work by virtue of Richard training others."

By translational work, Slayman means conducting fundamental scientific studies and applying that knowledge to clinical questions. Flavell explains: "I would say a high proportion of it is curiosity-driven, pursuing such basic questions as 'How does the body work?' But we always study this using diseases that matter. And what we try to do is to force ourselves to ask the question, 'Is this an important problem?'

"We want to study only important problems," he says, meaning problems that are fundamental or relevant to human disease. "You can spend your life doing unimportant things and in both cases you will spend just as much energy and get just as tired and as frustrated—and you'll be a lot less productive."

Finding motivation

In the late 1950s, when he was a rock 'n' roll-crazed teenager in the English county of Norfolk, no one would have mistaken Flavell for a budding academic. "I was a totally unmotivated student, except for the one thing I was interested in at the moment," he says. "First it was French, then it was history. Anything I was obsessed about, I was the best student in the class. For the rest I was in the bottom 25 percent."

That changed when he nearly failed his O-level exams, an essential step on the road to a university education in Britain. Raised in a family of teachers (his father was a school principal and a pilot during World War II), Flavell says the shock of a poor grade roused him from his scholarly indifference. Around the same time, thanks to an exceptional teacher, he discovered chemistry. After earning bachelor's and doctoral degrees in biochemistry at Hull, Flavell did postdoctoral work in the Netherlands and Switzerland and then joined the faculty of the University of Amsterdam. From the Netherlands, he moved to London, where he was head of the Laboratory of Gene Structure and Expression at the National Institute for Medical Research at Mill Hill. Then came an offer to join a commercial enterprise, the biotechnology startup Biogen, in Cambridge, Mass. "It was a very difficult decision, because I was totally satisfied with what I was doing. ... And along comes this crazy opportunity, which was also great because it was at a time when a new industry was being created." It was exciting, Flavell says—"You're alternately up in the clouds or on the precipice"—but when then-Yale Dean Leon E. Rosenberg, M.D., came looking for someone to head the medical school's new program in immunobiology, he decided he was ready for a return to academia. Biogen's next phase of growth, in which it would bring its first drugs to market, was a decade-long proposition. "I thought, 'Do I want to commit the next 10 years to doing that?'" he says. "I decided that I wanted to be more of a scientist and less of a manager."

At Yale, Flavell has struck a balance between the pursuit of basic biological questions and the pursuit of solutions to the causes of human disease. During its 20 years, the immunobiology department has opened major new areas of understanding, in particular discoveries establishing that the long-ignored innate immune system plays a much more significant role in the body's defenses than previously thought. Overturning assumptions that had stood for decades, department members Janeway and Ruslan Medzhitov, PH.D., demonstrated in *Nature* in 1997 that the innate response is the activating factor for the adaptive immune system's release of T- and B-cells.

"It was like saying there are only four planets in the solar system and then one day somebody comes along and says, no, there are eight," says Schatz. In the dozen years since the Medzhitov-Janeway paper appeared in *Nature*, a new branch of immunology research has been established, with hundreds of scientists looking for drug and vaccine targets among TLRS.

To help speed the clinical application of its basic immunology findings, the department launched a new program in 2007 called Human Translational Immunology (HTI), bringing together scientists from across the medical school and university to focus exclusively on research that could lead to better treatment of disease. The group studies the immune components of a wide range of disorders, including autoimmune diseases, cancer and the immune rejection of transplanted organs.

A better mouse

In the three years since the Gates project began, Flavell's group has made steady progress toward developing a mouse with a functional human immune system for the purposes of testing vaccines. His collaborator in Switzerland, Marcus Manz, M.D., of the Institute for Research in Biomedicine in Bellinzona, established the basis for the project in 2004, when his group created a mouse with human T-cells, B-cells and natural killer cells (NK cells target and destroy other cells that are infected with viruses or bacteria or are cancerous). To do this, they began with an immunodeficient mouse lacking RAGI or RAG2—genes needed for generation of B-cells and T-cells—and lacking the receptor required for the growth of the NK cells. When they injected human stem cells from umbilical cord blood into the liver of the mouse, those stem cells found their way to the bone marrow and began to develop into mature human immune cells.

"It is hard to believe that a human system may settle down in the organism of a mouse, yet the evidence points that way," Manz's colleague Elisabetta Traggiai, PH.D., said in 2004. "Two months since the transplant into the mouse, we have observed fully fledged human cells capable of reacting to human viruses and vaccines."

One problem that emerged, says Elizabeth E. Eynon, PH.D., who manages the Gates project as a research scientist in Flavell's group, was that the human cells did not mature properly. They did not have the expected longevity, they did not multiply in sufficient numbers and they did not interact with other cells as expected.

Eynon says those problems can be attributed to the lack of human growth factors and other molecules required by the T-cells and B-cells to develop correctly but not present in the mouse. "We tested to see how much alike a number of different factors were in the mouse and human and found about a dozen with significant differences," she says. Thus began the current effort to "knock in" the genes for those molecules and create the support system the human immune cells will need to thrive in the mouse.

In that work, the project has drawn on the expertise of Sean Stevens, PH.D., and others at Regeneron Pharmaceuticals in Tarrytown, N.Y. Regeneron created a highly efficient technology for knocking out genes and inserting human replacements into mouse DNA. Eynon says they are now working on introducing genes for the human major histocompatibility complex, which the body relies on to recognize foreign cells.

"What we hope to have [by July 2010] is a mouse that pretty nearly recapitulates the basic, fundamental immune responses that are human. All the appropriate cells will be there in the appropriate amounts, the cells will live a long time and the immune response will be functional," she says. "It certainly won't be the perfect mouse, but we think that it will make enough of an improvement to make this a useful model, not only for our lab but for other groups as well." YM

Michael Fitzsousa is director of communications at the School of Medicine.



Roots, Rock, Regale

When a young Richard Flavell and his bandmates were playing parties and clubs in England in 1960, they dressed in smart suits and thin ties and soaked up every bit of American blues and R&B they could get their hands on—including the music of Little Richard, Jerry Lee Lewis and Elvis Presley. Last May, Flavell was thrilled to meet a more famous contemporary of the English music scene, when Sir Paul McCartney visited Yale to receive an honorary degree.

At a reception in New Haven, Flavell told McCartney about his days playing clubs in Norwich, England, where early Beatles collaborator Tony Sheridan was a performer. Flavell remembers a conversation with Sheridan, who had just come back from Hamburg and a series of gigs with a new band from Liverpool.

"They've got a funny name," Sheridan told Flavell. "You should remember them. They're going to do well."

McCartney, says Flavell, was amused.



Online: Yale Netcasts Richard Flavell: Mouse With a Human Immune System Could Revolutionize Research

Online: Yale Netcasts Ruslan Medzhitov: Arming the Immune System



When scientists become artists

An ongoing exhibit of interesting scientific images raises the question of what constitutes art.

By Jenny Blair



PREVIOUS PAGE In this view of human tonsil tissue, scientists used green labels to locate naïve B lymphocytes, red for mature B cells and blue for a chaperone molecule. They then captured the image with a confocal microscope. ABOVE Purkinje cells from an adult mouse, located in the cerebellum and among the largest neurons in the brain, were stained red for acetylcholine receptors and green for DNA. The image was captured with a Zeiss Laser Scanning META microscope.

Image by Cécile Chalouni

Outside a third-floor elevator at the Brady Memorial Laboratory, four unusual prints are displayed on the wall. Each is a square filled with a dense and intricate pattern that resembles television static; the prints are identical except for different bright hues. Their striking texture and colors invite a long examination. They would not look out of place in an art gallery.

Or would they? The patterns represent a DNA microarray, and they were created by scientists working with David F. Stern, PH.D., professor of pathology, and by Terry Dagradi, a photographer and image specialist in information technology at the medical school who curated the display. The images are just a few of the many that Dagradi solicited from School of Medicine researchers as part of an ongoing project sponsored by the Office of Facilities Operations to display interesting scientific images in the corridors of the medical school. The Stern images are among the few that Dagradi altered (she added color), but in each case she played an artist's role herself in choosing, framing and arranging the images. "There is a pattern and a rhythm" to these images, said Dagradi. "Somebody made a visual decision."

Along with facilities manager Lorraine Roseman, Dagradi had already co-founded and curated ArtPlace, a project that since 2000 has shown the work of local artists, including many medical school faculty, on the walls of the Yale Physicians' Building (YPB) on Howard Avenue. But unlike in the YPB galleries, which exhibit portraits, landscapes and abstracts in various media, the laboratory images were made in the course of scientific research-mostly with microscopes. For example, in the Bridge Gallery at The Anlyan Center (TAC), which runs along a second-floor walkway that connects the center with Brady Memorial Laboratory across the street, passersby are momentarily arrested by a fluorescent tick; by a protein rendered as writhing arrows, bulges and ribbons; by a 15-day-old mouse fetus, its snout and nail beds picked out in delicate blue, a portrait as tender as the sight of a sleeping child; by a set of neurons done in soft blues, pinks and greens that look like impressionist pastels, the cells seeming to strain upward like so many flowers in a Monet painting. Images like these straddle an uncertain boundary between scientific representation and the fine arts, and for some viewers they raise the question, what is art?

For as long as scientists have made observations, they have illustrated them. Andreas Vesalius, the 16th-century pioneer of the study of anatomy, took apart and reassembled the human body in allegorical poses; Robert Hooke, the English polymath and contemporary of Isaac Newton, drew a flea seen under a microscope; John James Audubon, the 19thcentury American naturalist and ornithologist, painted birds at a Louisiana plantation. The stunning images that resulted might be called ancestors of the ones at the medical school.

"When I look at those 17th-century images, I don't hesitate to think of them as artworks," said Jonathan Gilmore, PH.D., assistant professor of philosophy and a critic for publications including *Art in America* and *Artforum*. "[Hooke is] not just showing you these things as they looked under the microscope—he's saying something about how marvelous or wondrous they are. ... There's no reason not to call that art."

That quality of wondrousness is one reason why such images still seem so much at home in galleries; moreover, what Yale is doing isn't new. Princeton University, for example, has become noted for its Art of Science competitions, in which organizers ask researchers to submit scientific images. More than a hundred Princetonians entered the first contest in 2005. The results, displayed in both a gallery and online, were so breathtaking that they caught the attention of *Wired* and *Science* and answered the contest's challenge: "Science Is Boring, Art Is Stupid, Prove Us Wrong."

"What's interesting to us is that these marvelous images ... come out of a process that is not really directed at making something beautiful," said Gilmore.

The portrait of the fluorescing tick is the work of Ruth R. Montgomery, PH.D., senior research scientist in medicine (rheumatology). She is also director of the confocal microscopy facility at the Department of Internal Medicine, where images are integral to her research. "As a person interested in how cells function, I've always taken pictures of them as part of displaying the research questions," she said. "You learn as a skill of the trade how to get a good image that can be used in manuscripts and in slides to demonstrate your point."

Montgomery studies what tick saliva does to human macrophage cells. "We were trying to trace a fluorescent marker through the tick to show which compartment of the tick it ended up in," she said, describing an image that graced not medical school hallways, but the cover of the *Journal of Experimental Medicine* in June 2006. "We never did find the actual molecule we were looking for, so we didn't really prove the point that we wanted to, but we got this cool picture. ... I figure [the display in TAC is] my one and only art opening for my lifetime."

Vali Gazula, PH.D., an associate research scientist in pharmacology, made several images of a mouse cerebellum. Because they were not intended for scientific publication, he manipulated their colors to make them more striking. "Since this is for art," he said, "I can put some dye more, some dye less, make [them] visually appealing." Gazula said he sometimes uses leftover reagents to create images in addition to the ones he needs for his research. "When Terry asked me for





Ticks from the *lxodes* family, the vectors for Lyme disease, were microinjected with fluorescent dyes to label surface structures and midgut cells. The images of the living ticks were made by laser scanning confocal fluorescent microscopy 24 hours after the dyes had been injected.



TOP Another view of Purkinje cells from an adult mouse cerebellum.

ABOVE Stains on this human colon section show actin filaments in green, an adhesion molecule on membranes of the colon's epithelial cells in red and the nuclei in blue. these pictures, I already had a lot of pictures, because I wanted to put them on my computer as screen savers."

Yet the native of Hyderabad, India, does not think of himself as an artist. He thinks of art in a more traditional sense and dislikes abstract art. His favorite artist is a 19thcentury Indian painter, Raja Ravi Varma, who painted episodes from the Indian literary epics in an academic European style.

One reason why the question "Is this art?" is so important, said Gilmore, is that the answer has some bearing on how we respond to the images. "If the scientists making them thought of themselves as creating works of art, that says that we should interpret them, perhaps look for meaning in them." Such works also get a pass on manipulation and enhancement—in art, anything goes. But the same is not true of images intended to demonstrate a scientific point; and indeed, other scientists whose works are on display deny having manipulated their images.

"Was it modified? No, not at all," said Marc Pelletier, PH.D., a former postdoctoral fellow who now runs a biotech company in Cleveland, of his transmission electron microscope image. It depicts a molecule of apolipoprotein A-I, part of the high-density lipoprotein type of cholesterol. As the image caption points out, the micrograph is reminiscent of the work of the Russian painter Wassily Kandinsky, a pioneering abstract artist of the early 20th century. "I framed it in the scope to have the look of the Kandinsky," he explained.

Though Pelletier didn't alter or shape his image as an artist probably would, that nod to Kandinsky was an act of craftsmanship. In general, however, if a scientist never intended an image as art, it may not be. "Whether something is a work of art or not—that question has to be sensitive to the context in which it was created," said Gilmore. "That doesn't mean that these can't be works of art made by, say, the person who collated them and put them together and used them." In some cases—and in a long tradition of "found" art—Dagradi herself may be the artist. She chose images that were intended only to demonstrate a scientific point and, by making a visual decision of her own, elevated them to the status of art by displaying or altering them.

"I think that one should be at least careful about identifying the scientists—those who just happened to have these images around [and] made them for research purposes—as artists, because the concept of art didn't enter into the process by which they made these things," said Gilmore. We sometimes honor people who create visually interesting objects, he explained, by calling them artists. "Are those people artists in the sense in which Rembrandt was an artist? Probably not. I think that would be a mistake."

Of all the scientists represented in Yale Med's galleries, Cécile Chalouni, PH.D., a former associate research scientist in the Department of Cell Biology who now works at Genentech in San Francisco, may be the most at home in the art world. Trained as an immunologist, she chose her field in part for the opportunities for imaging it affords; she was already an experienced aesthetic photographer when she began her doctoral studies. One of her microscopic images won a contest in *Nature Cell Biology* and three others appeared in the 40th edition of *Gray's Anatomy*, while her fine-art photography has been displayed in exhibitions in the United States and France.

Both science and art, said Chalouni, feature connections between very different things. What shows up in a frog's immune system is often seen in a human's as well, while an artist may create a visual image based on a piece of music. "This is something for me that is totally amazing—that you translate and make bridges between senses."

Asked if the images she chooses for display were originally done for the sake of beauty or for science, she said they were done for both. Like Gazula, Chalouni occasionally makes and saves extra images in the course of her work. "The images I kept have the scientific information I'm looking for, and possibly aesthetic elements. What is important to remember is that a less beautiful image can be scientifically more interesting than a very beautiful image." That is, dendritic cells like the one on TAC's wall—a blue many-armed star—may be visually appealing, but a micrograph of simple round lymphocytes may be more striking to a scientist if it illustrates an important discovery. To a scientist, the beauty of an image may be more than visual. Yet, as artists have always known, the visual element makes for powerful demonstrations and may be the most effective mode of scientific communication.

IND RPOAL

"A fundamental driving force in science is to look for the beauty in nature," said Pelletier. "So scientists ... should have an eye to explore that nature." If the images in Brady and TAC are any indication, Yale scientists' eyes are wide open.

Pioneering scientific image-makers like Hooke who looked through their microscopes were filled with wonder at what they saw, and their modern-day counterparts—as well as many nonscientists—continue to gaze upon the natural world with awe and appreciation. "Sometimes there's no urgency in deciding whether or not these are works of art," said Gilmore, "because these things are just incredibly marvelous to look at in their own right." YM

Jenny Blair, M.D. '04, is a physician and writer based in New Haven.



This embryonic mouse is about 15 days old. A marker has been inserted and blue dye will stain any site in which the *lacZ* gene is normally expressed. In this image, the dye marks hair follicles that are forming, the nails and the epithelium around the nose and mouth.



Thomas Lynch

Lung cancer expert to lead cancer center

THOMAS J. LYNCH JR., M.D. '86, a lung cancer expert at Massachusetts General Hospital (MGH) and Harvard Medical School, was named director of Yale Cancer Center (vcc) in February. Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, announced the appointment, which was effective April 1. Lynch will also serve as physician in chief of the new Smilow Cancer Hospital at Yale-New Haven.

In accepting the new post, Lynch said that he wants the cancer center to be known for discovery; personalized cancer therapy; the importance of compassionate patient- and family-centered care; and a commitment to quality, safety and outcomes measurement.

"One of the reasons why we're not curing cancer today is that we need to better understand the biology of cancer," said Lynch, who served as chief of hematology/ oncology at MGH Cancer Center. "Yale is well-positioned for that, with expertise in immunobiology, genetics and tumor biology. At Yale, the scale is right for an integrated cancer program between science and clinical medicine. You have laboratories where fundamental discoveries are being made-within a couple hundred feet of clinics where patients are being treated—and people who are active in the pursuit of both clinical excellence and scientific discovery."

As part of that integration of science and clinical medicine, Lynch will oversee a new institute for cancer biology at the university's 136acre West Campus. He will recruit a director and a team of scientists specializing in cell signaling, cancer immunology, and drug development and target acquisition for the new institute.

vale medicine spring 2009

Other major plans for vcc and Smilow Cancer Hospital include recruitment of clinicians and translational researchers, a significantly expanded clinical trials network and a program that will provide molecular profiling services to enable targeted therapies.

As director of the MGH Thoracic Oncology Center, Lynch made important contributions to developmental therapeutics and defining the optimal treatment for patients with lung cancer. He has pioneered the use of molecular testing for mutations in the epidermal growth factor receptor gene to select patients who can benefit from targeted lung cancer therapies.

Lynch succeeds Richard L. Edelson, M.D. '70, chair and the Aaron B. and Marguerite Lerner Professor of Dermatology, who became YCC director in 2003. Edelson will continue as chair and professor of dermatology. NOTES





Several faculty members have

been named to endowed chairs

Caplan, M.D. '87, PH.D. '87, FW

'89, known for his research on

the sorting and function of ion

proteins in polarized epithelial

Professor of Physiology. His

the proteins that interact with

ion transporters to determine

properties. He is currently the

their localization and trafficking

interim chair of the Department

of Cellular and Molecular Physiol-

ogy. Mark Hochstrasser, PH.D.,

was named the Eugene Higgins

Professor of Molecular Biophysics

and Biochemistry. Hochstrasser's

intersection of biochemistry and

genetics, attempts to understand

protein turnover at the molecular

which specific proteins are rapidly

degraded within eukaryotic cells,

newly designated the David Paige

other skin cancers using the Mohs

micrographic technique. Leffell,

who is also chief executive officer

of Yale Medical Group, has served

as deputy dean for clinical affairs

2005. David A. McCormick, PH.D.,

was named the Dorys McConnell

Duberg Professor of Neurobiolo-

and network mechanisms of the

to attention, working memory,

sleep-related activity and visual

gy. McCormick studies the cellular

brain's cortical function in relation

perception. **Scott A. Strobel**, PH.D., was named the Henry Ford II

Professor of Molecular Biophysics

and Biochemistry. His labora-

tory employs such technologies

at the School of Medicine since

Smith Professor of Dermatology,

specializes in the diagnosis and

treatment of melanoma and

level—particularly the ways in

even while most proteins are

spared. David J. Leffell, M.D.,

research, which lies at the

cells, was named the C.N.H. Long

laboratory focuses on identifying

in recent months. Michael J.





David Leffell

David McCormick

as organic synthesis and X-ray crystallography to study reactions catalyzed by RNA.

Three neuroscientists have been named to endowed chairs funded by an alumnus of the Yale College Class of 1928. Angus C. Nairn, FW '82, PH.D., who was named the Charles B.G. Murphy Professor of Psychiatry, is noted for his research on the molecular actions of dopamine in the basal ganglia. Nairn has extensive experience in enzymology, protein chemistry and the molecular biology of signal transduction, particularly with respect to the role of protein phosphorylation in the nervous system. Marina R. Picciotto, PH.D., was named the Charles B.G. Murphy Professor of Psychiatry. She specializes in molecular neuroscience, behavioral pharmacy, mouse genetics and translational neuroscience. The goal of her research is improved understanding of the role of single molecules in complex behaviors related to addiction, depression and learning. Jane R. Taylor, PH.D., was named the Charles B.G. Murphy Associate Professor of Psychiatry. She specializes in brain research related to drug addiction and such psychiatric disorders as ADHD, depression, schizophrenia and Tourette syndrome.

Vikki Abrahams, PH.D., assistant professor of obstetrics, gynecology and reproductive sciences, has received a 2009 Albert McKern Scholar Award for Perinatal Research. The two-year award of \$100,000 per year will fund her proposal, "Human Endogenous Retroviruses: A Novel Biomarker for Pre-eclampsia." The award is funded by a bequest from Albert McKern, M.A. '13, M.D., an Australian who studied engineering





Scott Strobel

at Yale before entering medical school at the University of Edinburgh.

Joshua A. Copel, M.D., professor of obstetrics, gynecology and reproductive sciences and of pediatrics. has been named president-elect of the Society for Maternal-Fetal Medicine (SMFM) for the coming year. The appointment begins in February 2010. The SMFM is a nonprofit organization of more than 2,000 members dedicated to improving care for pregnant women and their fetuses. The society's primary objectives are to promote and expand education in maternal-fetal medicine and to encourage the exchange of new ideas and research concerning the most recent approaches and treatments for obstetrical problems. Copel received the Dru Carlson Award for Research in Ultrasound and Genetics from the SMFM in 2007.

Walter S. Gilliam, PH.D., assistant professor in the Yale Child Study Center and director of its Edward Zigler Center in Child Development and Social Policy, received the Priscilla Canny Research Award in December at Connecticut Voices for Children's 8th annual First for Kids awards ceremony. He was recognized for providing consultation to state and federal decision makers. Connecticut Voices also praised his dedication to research on translating early-childhood policies into effective services and improving the quality of pre-kindergarten and child care services, as well as studying the impact of earlychildhood programs on children's school readiness. Gilliam was a principal investigator of the National Pre-Kindergarten Survey, the first-ever national study of the



Picciotto



Jane Taylor

implementation of state-funded

Robert Heimer, PH.D., professor of

epidemiology (microbial diseases)

and pharmacology, will work and

lecture in Russia this year with

support from a 2009 Fulbright

Scholarship, Heimer's project,

"Delphi Analysis to Explore the

Among Russian Drug Users," will

be conducted at Kazan State Medi-

from March through July. Heimer's

research efforts include investiga-

tion of the mortality and morbid-

ity associated with injection drug

use. He is director of the Interdisci-

plinary Research Methods Core at

Yale's Center for Interdisciplinary

the Yale office of the Connecticut

Gregory L. Larkin, M.D., professor

of surgery (emergency medicine)

and associate chief of emergency

medicine, has been awarded a

two-year American Foundation

guished Investigator Award for

his study, "Suicide Clusters Across

for Suicide Prevention Distin-

the Globe: Geospatial Trends

in America, Ireland and New

the New Zealand Ministry of

in that country. Larkin has also

as chair of the Task Force on

Zealand." This award extends a

recent grant Larkin received from

Health to examine suicide clusters

recently formed and been named

Emergency Medicine and Suicidal

Behavior of the International As-

sociation for Suicide Prevention.

Gil Mor, M.D., and Alessandro

Santin, M.D., members of Yale

Cancer Center, received more

than \$5 million in federal and

improve detection of ovarian

foundation grants in January to

Research on AIDS and director of

Emerging Infections Program.

Origins of the HIV Epidemic

cal University in Kazan, Russia,

pre-kindergarten programs.

Joshua Copel



cancer and to find a cure for the

disease. Santin received \$1.7 mil-

lion, including two grants from

of Health and another from the

National Cancer Institute (NCI) for

\$346,000 per year for five years.

peutic vaccination strategies for

the treatment of HPV-infected

cervical cancer patients, he also

studies therapies for the manage-

ment of chemotherapy-resistant

Mor will use an NCI grant of

\$314,000 per year for the next

five years to better understand

cancer cells resist cell death.

the mechanism by which ovarian

Another newly awarded five-year

NCI grant totaling \$1,715,000 will

fund Mor's research on the ways

immune system to promote their

own growth and progression. Mor

also has three foundation grants

that include \$150,000 per year for

three years from the Janet Burros

Memorial Foundation; \$50,000

per year for three years from the

Sand Foundation; and \$50,000

Pasquale Patrizio, M.D., direc-

tor of the Yale Fertility Center

gynecolo-gy and reproductive

sciences, addressed the Italian

Parliament in Rome in January on

a 2004 Italian law that restricts in

vitro fertilization (IVF) practices.

According to Patrizio and other

pregnancies and higher rates

insemination to three eggs

per patient-if all three eggs

result in fertilization, all three

embryos must be transferred for

implantation. The law also bars

genetic screening to prevent the

experts, the law has led to fewer

of multiple births. The law limits

and professor of obstetrics,

from the Adler Foundation.

in which tumors influence the

ovarian cancer.

Although Santin's NCI-funded

research is focused on thera-

the Italian National Institutes



Walter Gilliam

Gregory Larkin

Majid Sadigh

transfer of embryos with lethal or severely disabling diseases. As a result. fewer Italian women are getting pregnant through IVF on their first try, causing them to go through multiple IVF cycles. Patrizio hopes that he convinced the legislature that the law does a disservice to Italian women and also encourages couples to seek fertility treatments in countries with less restrictive legislation.

Maiid Sadigh, M.D., associate professor of medicine, was nominated by medical students for the Humanism in Medicine Award presented annually by the Association of American Medical Colleges. The award recognizes a medical school faculty physician who exemplifies the qualities of a caring and compassionate mentor in the teaching and advising of medical students. The candidate must also possess the desirable personal qualities necessary to the practice of patient-centered medicine. Although Sadigh was not named this year's recipient, he received a plaque in honor of his nomination. In addition to his duties at Waterbury Hospital, Sadigh directs the Makerere University-Yale University collaboration that sends medical students and physicians to Mulago Hospital in Uganda for rotations. The students wrote in their nominating statement that Sadigh "has been a source of inspiration and guidance to the many medical students he has encountered. both on this continent and on continents far away."

SEND FACULTY NEWS TO

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At Commencement, the PA Program's history

Alfred Sadler, the first director of Yale's Physician Associate Program, described its early days in the 1970s.

When Yale's Physician Associate Program was launched in 1971, 28 of the 30 members of the Class of 2008 had not yet been born. At their Commencement in December the graduates got a history lesson along with their diplomas. The lesson came firsthand, delivered by the co-founder and first director of the Yale program, Alfred M. Sadler Jr., M.D.

Physician associate programs have their roots in emergency care, and Yale's began as an experiment. "We were designing the curriculum as we went along," Sadler said.

The Class of 2008 reflects the growth of the program in both numbers and scope. Whereas Yale's first graduating class of just five students left with a certificate in physician associate studies in 1973, this year's class—like others since 1999—earned a master's degree in medical science, the M.M.SC. Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, said the program was lengthened from two years to 28 months under his tenure, "which is why we're having Commencement on this freezing day" in December.

Sadler said the Yale program came into being when he and his twin brother organized regional emergency



ABOVE The 30 members of the physician associate Class of 2008 heard about the history of the Yale program from one of its founders, Alfred Sadler Jr., who addressed the class at Commencement in December.

RIGHT Graduates Adam Cohn, Song Jin Comstock and Rachelle Concepcion read the professional oath of physician associates.



medical services in Connecticut, creating a model that was copied nationwide. Meanwhile, Jack Cole, M.D., chair of surgery, had received a grant from the Commonwealth Fund to start a trauma program within the Department of Surgery. He and Sadler had both noticed that the military had produced army medics competent to treat trauma alongside doctors, and that "these professionals were actually practicing medicine," Sadler said. The two men then convinced Yale to create "the medical school's first experiment in nonphysician education."

Sadler, who directed the program until 1973, spearheaded legislation to authorize physician associates to practice medicine in the state of Connecticut. As inaugural president of the Association of Physician Assistant Programs, he helped develop accreditation standards for the profession and worked with the National Board of Medical Examiners to create the first national board examination.

Yale has since graduated 895 students from the program. Today there are 142 programs nationwide, Sadler said.

At the Commencement ceremony William B. Stewart, PH.D., associate professor of surgery (gross anatomy), and Shanta E. Kapadia, M.B.B.S., lecturer in surgery (gross anatomy), received the Didactic Instruction Award from students. Gerard J. Kerins, M.D., geriatrics section chief at the Hospital of Saint Raphael, received the Clinical Instruction Award for a clinical rotation site that provides exemplary teaching. The Jack Cole Society Award, for contributions in support of the physician associate profession, went to Paul P. Possenti, PA-C, lecturer in surgery (trauma).

Adam Cohn, PA '08, received the Dean's Award for Academic Achievement. Arielle Macher, PA '08, received the Dean's Award for Clinical Excellence, and Lauren Myers, PA '08, received the Dean's Humanitarian Award. —John Dillon

BELOW The Class of 2011 took affectionate potshots at faculty in February with their secondyear show, "The Great ST Depression." Ripped from the headlines, the show's plot revolved around efforts to keep the School of Medicine functioning during an economic decline.

U.S. economy in free fall! Yale endowment down! Med school scrambles for \$\$\$!

Carrying on a 6o-year-old tradition, the second-year class mocked its teachers and mentors with irreverence and affection at their show in February, "The Great ST Depression."

The show's 16 sketches centered on a loose plotline based on current events: the School of Medicine has lost its endowment and the dean is laying off faculty and eliminating financial aid. Entering survival mode, faculty and students must get part-time jobs—at s'wings or the Cedar Street food carts, for instance—or as Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, suggests in one sketch, by holding up and robbing s'wings, a Crown Street eatery.

The cast of characters was familiar. Associate Dean for Student Affairs Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93; Alpern; and Margaret J. Bia, M.D. (played by Larissa Chiulli, Derek Kennedy and Lauren Hackney, respectively) all received considerable skewering. Standout moments included the song "Docta Bia," based on ABBA's "Mamma Mia" and Jennifer Lopez's "Jenny from the Block"; a video sketch featuring Shanta E. Kapadia, M.B.B.S., dishing up Indian food at a cart on Cedar Street; and the song "My Goodies/ Rizzilicious," featuring Matthew Singleton on stage and Carl Berdahl as the voice of Lawrence J. Rizzolo, PH.D., based on Ciara and Petey Pablo's "My Goodies" and Fergie's "Fergilicious."

Other highlights included a 14member orchestra; a video parody in which David L. Katz, M.P.H. '93, M.D.,





played an overadrenalized juice fanatic; and a video screening of the Class of 2011's class prank—a parody of a *Saturday Night Live* sketch about bodily functions in which faculty made faces of delight or disgust. "Our faculty had a great sense of humor and recognized that we only make fun of them out of love and respect," said Patricia Peter, one of the show's two executive producers.

Planning for the show began last summer, and about 90 of the class' 100 members participated. "We're very proud of how collaborative it was," said co-producer Janet Chiang. Henry Park directed the show.

-Charles Gershman



ABOVE LEFT Gisella Weissbach-Licht, played by Lauren Graber, chastises faculty members James Jamieson, played by Ben Goldberg, and Michael O'Brien, portrayed by John Thomas, for spending too much money and getting the medical school into a financial crisis.

ABOVE RIGHT A highlight of the show was "My Goodies/Rizzilicious," featuring Matthew Singleton as anatomy professor Lawrence Rizzolo. The number was based on Ciara and Petey Pablo's "My Goodies" and Fergie's "Fergilicious."

Alum finds fascination in disease and the end of life

Robert Buckingham's career has taken him around the world as he studies HIV/AIDS, prostitution and hospice care.

Robert Buckingham, PH.D. '78, saw a lot of people die when he served in the U.S. Navy during the height of the Vietnam War. But he was more drawn to illness-related mortality, even in



Robert Buckingham, an epidemiologist at New Mexico State University's College of Health and Social Services, works around the world on AIDS prevention among sex workers and has been instrumental in developing hospice care. combat zones. "In my travels throughout Southeast Asia during the war, I saw a lot of disease and death," he said. "I got fascinated with diseases."

Buckingham's career has run on the tracks of disease and death ever since. Usually the tracks are parallel, but they have also diverged and intersected, frequently taking him back to the places in Southeast Asia where his interest was first sparked.

For Buckingham, an epidemiologist and professor of health science at New Mexico State University's College of Health and Social Services, the intersection became personal as he entered the School of Public Health in the 1970s. His mother had just died of breast cancer, "so I was interested in the care she got—and the lack of care." His frustration over the hospital's aggressive attempts to keep her alive instead of alleviating her suffering led him to become involved in palliative treatment.

At the same time, the late Florence S. Wald, R.N., the former dean of the School of Nursing, was trying to establish the first inpatient hospice in the United States. Under Wald's tutelage, Buckingham helped to write a grant proposal that led to funding for hospice care. In researching his doctoral dissertation, he came to the conclusion that care for the dying was better in a hospice than in a hospital.

The Connecticut Hospice opened in Branford in 1974. Today there are about 8,000 hospices around the world (including more than 4,500 in the United States), according to Stephen Connor, PH.D., vice president of research and international relations at the National Hospice Foundation. Buckingham had a hand in developing

about 90 of them. "Bob is remarkably intelligent and capable," Connor said. "He certainly is someone wellregarded in the field."

Buckingham moved on to other areas of public health, notably HIV/ AIDS prevention among sex workers. He returned to Thailand as the AIDS epidemic spread and has since studied condom use among prostitutes in that country's commercial sex industry and started a pediatric hospice for children with AIDS there. He spent the 2000-2001 academic year "developing programs for commercial sex workers as well as treatment programs for workers who were HIV-positive." Before his research began, only 11 percent of sex workers' clients had used condoms. His study, published in the journal AIDS Care in 2005, found that the rate had risen to 51 percent. It wasn't ideal, but in some brothels as many as 89 percent of the workers' clients use condoms, and overall the HIV rate in Thailand has "decreased significantly," he said. Buckingham concluded that more focus needs to be put on native Thai patrons, who are less likely to use condoms than Western or other Asian customers.

Buckingham is trying to transfer that model of HIV prevention to prostitution in Latin America. One such place is Ciudad Juárez, Mexico, just across the border from El Paso, Texas, and not far from his campus in Las Cruces, N.M. "When you see poverty you see prostitution, and when you see prostitution you see disease," he said. He has encountered little opposition from the authorities, even though Mexico is a heavily Roman Catholic country. "We usually don't get interference," he said. "We're trying to help." Most recently, Buckingham has been asked by the government of Honduras to form the country's first health commission. The need for health care is acute, especially for people living on the islands off the coast where care is "nonexistent," he said. "What we're doing is a simple needs assessment affecting the country." He plans to get the project in full swing while on sabbatical in 2009-2010.

Honduras also has a disproportionately high share of Central America's HIV/AIDS cases—some estimates have it as high as 60 or 70 percent—so Buckingham will work to promote condom use there. He will also likely be working with the dying, because he helped to establish a hospice in that country.

His work with hospices and sex workers isn't all that divergent, he said—in fact, the two tracks crossed one day in Thailand. He was interviewing prostitutes when a woman, wrongly assuming that he was a physician, begged him to care for her sick infant. "I said, 'I can't take care of your baby,' and gave it back to her. She said, "No, no!' and just ran away. We brought it to the medical school. Sure enough, the baby was HIV-positive. Word went out that I found a place for these dying kids."

Buckingham helped set up a hospice there, too. "Life is weird sometimes," he said.

—John Dillon

An international traveler makes himself at home in the world's great libraries

Wherever **Stanley Simbonis**, M.D. '57, travels, he visits the local library. If it's Athens, you'll find him in the Gennadius Library at the American School of Classical Studies, or the archeological library at the British School at Athens, where he reads about the origins of language and writing. This research, of course, occurs after his annual sixweek course in the Greek language at the University of Athens.

"The library is the heart and soul of the university," said Simbonis, who is, not surprisingly, a trustee of the Cushing/Whitney Medical Library. "It's the guts of the university, the crown jewel. How can you do without it? It's been a storehouse of knowledge throughout the ages."

If it hadn't been for libraries, Simbonis might never have made it to the School of Medicine.

Born in Manhattan in 1928 to emigrants from Greece, Simbonis lived in a tenement apartment in the Bronx with his mother and brother; his father died when he was 8. Simbonis loved to look at the handful of books in his home until he discovered the public library on Washington Avenue; then he started to read everything from Churchill to calculus. At 13, when he finished school for the day, he wandered into the libraries and classrooms of Fordham University, where a chemistry professor allowed him to sit in on classes.

Simbonis' junior high school science teacher steered him to the Bronx High School of Science, which still enjoys a reputation as one of the best



Wherever Stanley Simbonis travels, he always makes a point of visiting the local library. "The library is the heart and soul of the university," said the retired pathologist, who is still an associate clinical professor at Columbia University's College of Physicians and Surgeons. "It's been a storehouse of knowledge throughout the ages."

college preparatory high schools in the country. He grew restless, however, in part because the school had no sports or even a gym at that time, and he dropped out at age 16.

"My original dream was to be a center fielder for the Yankees and then I tried to become a musician," he recalled. "Medicine was my third choice."

In the 1940s, trying out for a professional baseball team did not require an agent or experience. Simbonis just showed up at Yankee Stadium. He also took a crack at the Dodgers. Neither team hired him, so he knocked on doors all along Broadway to audition as a big band drummer. "I could barely keep a beat," he said. He did, however, meet bandleaders Louis Prima and Harry James.

Still uncertain of his career path, he took on three menial jobs, delivering newspapers on Wall Street at 5 a.m., running mail for a ship's broker and washing dishes at the Horn & Hardart automat. "The dishwashing really woke me up," Simbonis said. "I thought, 'What the hell am I doing here? It's obvious that I have to go to school.' The GI Bill sounded pretty good."

Simbonis enlisted in the Marine Corps on September 2, 1945, the day the Japanese surrendered to the Allied forces, and began to pursue his high school equivalency degree. Because he took more than a dozen of the academic classes the Marines offered, he was called to the Marine Corps school in Washington, D.C., to teach English.

Simbonis planned to go to Columbia University and live at home after leaving the service, but his mother had remarried and moved to New Haven. He followed her to the city and enrolled in Yale College. Simbonis lived off campus above the Sisk Funeral Home on Howe Street, where he earned \$25 a month and a free apartment for answering the telephone in the middle of the night. He majored in zoology and earned his undergraduate degree in 1953.

Simbonis then entered the School of Medicine, where he took an interest in pathology because it allowed time for research. After graduating he worked in the New York University lab of biochemist Severo Ochoa, M.D., who won the 1959 Nobel Prize for medicine or physiology for his discovery of an enzyme that can synthesize RNA. "Ochoa was brilliant, but also fun-loving," Simbonis remembered. "He bought a red sports car with his prize money."

After stops at Columbia University and Holy Name Hospital in Teaneck, N.J., Simbonis settled down at St. Joseph's Hospital in Paterson, N.J., where he became chair of pathology. He retired in 1992 but remains an associate clinical professor of pathology at Columbia University's College of Physicians and Surgeons, where he still audits classes.

Teaching, he said, was his greatest contribution to pathology. "I hope I was able to convey to students how to examine slides and specimens, and then *think* fiercely on how to synthesize the material at hand to arrive at reasonable conclusions," Simbonis recalled. "It wasn't an easy task but it was really worth the effort."

Since 1975 Simbonis has lived in a historic brownstone in Greenwich Village, where he is active in neighborhood preservation. Divorced, he has no children. He travels widely and owns an apartment in Athens. He also has a vacation home on Fire Island, N.Y., which he has willed to the School of Medicine. The home will be sold upon his death and the proceeds divided between the library and a scholarship to be set up in his name. It will be a fitting gift from a lover of libraries.

—Alix Boyle

A life in public health takes an alumnus around the world and back to Brooklyn

Research, teaching and other projects have exposed **Michael A. Joseph**, M.P.H. '96, PH.D., to Zimbabwean health crises, the Bedford-Stuyvesant–Crown Heights AIDS epidemic and tuberculosis (TB) affliction in South African provinces. No matter where he has traveled, however, he has always returned to SUNY Downstate Medical Center in Brooklyn, where his interest in public health began.

Joseph's wide-ranging path wasn't what he'd imagined growing up in Brooklyn. Although he had planned to become a doctor, the premed courses at Brooklyn College turned him away from medicine. He switched his major to health science and secured an internship at Downstate. Assisting the late Rachel G. Fruchter, M.P.H., PH.D., then-associate professor of obstetrics and gynecology, in researching gynecological cancers among minority and immigrant women, he said, "allowed me as an undergraduate to see a research project from inception to completion." It also connected him to the institution that would become his professional touchstone.

"By my second epi course, I fell in love with the hands-on detective work linking an exposure to a health outcome," recalled Joseph, who was encouraged by professors to pursue an M.P.H. At the School of Public Health he served as a teaching assistant during his second year, where his love affair with teaching began and spurred him toward a PH.D. Joseph's master's thesis was based on his analysis of Fruchter's data.

For his doctoral work, he went to the University of Michigan and assisted

in the teaching of master's-level biostatistics and epidemiology courses. There, he said, "I was trained by the best of the best in epidemiology: Siobán Harlow, Sherman James and David Schottenfeld." He continued exploring a theme from his Downstate internship minority health—for his dissertation, "Risk Factors for Lower Urinary Tract Symptoms in African-American Men."

Strong family ties lured Joseph back to Brooklyn after he had completed his doctorate and was looking for a faculty position. When he heard about



Michael Joseph initially planned to become a doctor, but instead he went into public health. His studies and his work have taken him around the country and to Africa, but he has always returned to his home in Brooklyn, where he focuses on AIDS and tuberculosis.

Downstate's new public health graduate program emphasizing urban and immigrant health—a marriage of the themes that have guided his career-it seemed like a natural fit. "At a wellestablished public health school, I'd have less input, less room for innovation and growth," he reasoned. "This was an opportunity to serve as a role model for a diverse student population." Joseph's lectures explore factors "prohibiting minority and underserved populations from engaging in healthy behaviorsincluding economic inequality, lack of employment opportunity, poverty and our failing health care system."

Dedicated to both teaching and minority health, Joseph was invited on three occasions to teach an intensive biostatistics and epidemiology course to public health students at the University of Zimbabwe in Harare. "Africa is plagued by many infectious diseases, so students are in the field tackling outbreaks. What I teach here over 14 weeks, I had to teach there in two, from 9 to 5 daily. It was exhausting but quite fulfilling," he said. Through Downstate's HIV Center for Women and Children, he was invited in 2008 to train HIV and TB researchers at South Africa's University of the Free State in Bloemfontein. "They had a wealth of data but needed assistance carrying out the next steps-conducting appropriate analysis or writing a manuscript for publication."

An assistant professor of epidemiology, Joseph is the junior principal investigator on a grant from the Centers for Disease Control and Prevention, in which Downstate faculty collaborate with the Arthur Ashe Institute for Urban Health to target sexual behaviors that put heterosexual African-American men at risk for HIV infection. In 2006, Joseph and his wife-to-be, Lauretta Ansah, used funding from the National Black Leadership Commission on AIDS to support a ministry to educate the members of Bedford Central Presbyterian Church about the disease. "For years, the black church was silent about the AIDS epidemic because of stigma. Many in the black community still believe it's largely a homosexual disease," said Joseph.

Joseph always reaches out to peers. At Michigan, he mentored several students, including members of the Public Health Students of African Descent, a student-run group that was established over 21 years ago. He tutored master'slevel students struggling with epidemiology or biostatistics. He also co-founded the Black Young Professionals' Public Health Network, also known as 'The NETWORK.' The NETWORK presents such programs for black attendees at American Public Health Association conferences as "Is Hip Hop Healthy for African American Females?" Poster sessions showcase research in health disparities by minority public health students and young professionals.

To Pascal J. Imperato, M.D., M.P.H., dean and Distinguished Service Professor of Downstate's Graduate Program in Public Health, "Michael is extremely skilled in teaching epidemiological concepts [so that students are] engaged and encouraged to reach beyond their own perceived limits. His introductory epidemiology course is one of the most popular in the graduate program." Joseph's students consistently give him top ratings as teacher, mentor and role model.

After interviewing at Downstate

in 2004, Joseph remembers thinking, "They loved me, I loved them, it's a great fit." For his work there, he was inducted into Delta Omega, the public health honorary society. Michael Joseph knows he's in the right place.

-Carol Milano

Familiar Faces

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



Lionel Nelson

1960s

Lionel M. Nelson, M.D. '69, writes from Camp Stryker in Baghdad, where he is a colonel in the Army and the brigade flight surgeon with Task Force 449: "I have been here a month now. and have fallen into the routine. The day starts at o dark 30 with my usual exercise routine. ... no different than home. I get to fly about once a week, usually something to attend to at one of our forward operating bases where we keep air crews, and a good excuse to get outside the wire and see some green fields. Parts of the Iragi countryside along the rivers are quite beautiful. Otherwise, most of the day is a combination of staff duties (coordination, reports, briefs, etc.), supervising medical care for the task force personnel and overseeing the medical portion of our medevac operations. I have a staff of 25, with several physicians to help me with this. **Operational tempo remains** quite heavy, but threat level is relatively low at this time. I came out of retirement (21 years in, mostly as a reservist, and retired for five years) to do this. The need for flight surgeons with experience is significant. The Army asked, and I volunteered. I will be here about 90-120 days, and have temporarily closed my ENT practice in San José, Calif., for that time. Although I have had other deployments in the past, this is my first time in Iraq. It is great to be back around the aviators. Helicopter crews, particularly the Apache and medevac folks, are full of bravado and practical jokes. I am glad to have the opportunity to be here and help take care of these very dedicated and brave Americans."



Merchant

Martin Wand, M.D. '67, was elected vice chair with succession to chair of the American Board of Ophthalmology. Wand is also the chair of the council and trustee of the 27,000-member American Academy of Ophthalmology. He specializes in glaucoma and remains in full-time practice with an eight-physician subspecialty group in Connecticut.

19705

Laura M. Finkelstein, M.P.H. '79, and Lawrence N. Rothbart were married on November 17, at the River Café in Brooklyn. Finkelstein is a quantitative and qualitative market research consultant based in Brooklyn, where she works with financial service companies, advertising agencies and consumer packaged-goods companies. Rothbart is a lawyer in Manhattan specializing in matrimonial and family law.

1980s

Juanita Merchant, M.D. '84, PH.D. '84, professor of internal medicine and of molecular and integrative physiology at the University of Michigan Medical School, was named to the Institute of Medicine of the National Academy of Sciences in October. She was also named an Outstanding Woman in Science for 2008 by the American Gastroenterological Association Foundation for Digestive Health and Nutrition, in honor of her contributions to digestive disease science.

1990s

Michael A. Coady, M.D., M.P.H. '97, has been named cardiac surgeon at The Miriam Hospital in Providence, R.I. He is also chief of surgery at Landmark Medical Center in Woonsocket, R.I.

20005

James M. Kessler, M.D., M.P.H. '01, was married to Jessica A. Bassik in Kings Point, N.Y., in November. Kessler is a third-year radiology resident at Jacobi Medical Center in the Bronx. He graduated summa cum laude from the American Jewish University in Los Angeles. He received a master's degree in public health from Yale and a medical degree from Johns Hopkins. His wife is a third-grade teacher at Public School 75 in Manhattan. John Strasswimmer, M.D., PH.D., HS '03, was part of a group that traveled to Malawi in September to assess the surgical needs of albino patients and to determine how dermatologic surgeons can help. Strasswimmer is a Mohs surgeon in Delray Beach, Fla.

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Rebecca L. Calderon, M.P.H. '81, PH.D. '86, died on December 21 at her home in Chapel Hill, N.C., after an 18-month struggle with lung cancer. Since 2004 Calderon served as director of the human studies division of the National Health and Environmental Effects Research Laboratory at the Environmental Protection Agency.

William A. Clermont, R.N., M.P.H. '57, died on December 22 at Fort Pierce Hospice House in Fort Pierce, Fla. He was 92. Clermont served as a medic in the U.S. Army in England during World War II and was a hospital administrator at Alice Hyde Memorial Hospital in Malone, N.Y.

Charles H. Crothers, M.D. '44, HS '48, died on January 10 of cancer at his home in Van Buren, Ind. He was 88. Crothers practiced pediatric medicine in Connecticut for more than 40 years. After serving in the U.S. Army in the Philippines, he returned to Grace-New Haven Community Hospital in 1948, where he was chief resident and assistant professor of pediatrics. In 1952 he began a private practice in New Britain, Conn.

Nicholas D. D'Esopo, M.D. '36, died on December 12 at his home in Woodbridge, Conn. He was 99. During the 1940s D'Esopo conducted studies that led to the development of combined chemotherapy for the treatment of tuberculosis. From 1953 until 1985, he was chief of the pulmonary disease service at the West Haven VA Medical Center. He was also a clinical professor of internal medicine at the medical school until 2004.

Rocko M. Fasanella, M.D. '43, chief of ophthalmology at

Yale from 1951 to 1961, died on February 11. He was 92. Fasanella established the ophthalmology residency program and headed the section when it was still within the Department of Surgery. He laid the foundation for ophthalmology's growth into a freestanding department with its own full-time faculty. He is known for a surgical technique that bears his name and is still widely performed, the Fasanella-Servat procedure for drooping eyelid, which was developed with Javier Servat, M.D. His popular textbook, Management of Complications in Eye Surgery, was a must-read in the 1960s and 1970s.

Francis R. Fekety Jr., M.D. '55, died at Parkcliffe Alzheimer's Community in Toledo, Ohio, on January 6. He was 79. After service in the U.S. Public Health Service and a teaching appointment at Johns Hopkins University, Fekety established and was named chief of the Infectious Diseases Division of the Department of Internal Medicine at the University of Michigan Medical School. He was on the faculty there from 1967 until his retirement in 1995.

Joanne E. Finley, M.D., M.P.H. '51, died on October 15 in Baltimore, Md. Finley was the commissioner of health in New Jersey from 1974 to 1982 and deputy secretary of health for the state of Maryland from 1983 to 1984.

Dennis R. Hamilton, M.P.H. '71, died on September 16 in New Hampshire of a heart attack. He was 66. A resident of New Haven, Hamilton was in New Hampshire working on a photo exhibit for Amman Imman, a project started by Ariane Kirtley, M.P.H. '04, to bring water to remote areas of the African country of Niger. Although retired, Hamilton was active in New Haven's progressive community and was associate director of Amman Imman. An accomplished pianist, Hamilton often played at his friends' birthday parties.

Edward H. Hon, M.D., HS '55, died on November 6 at his home in Bradbury, Calif. He was 89. Hon worked with Orvan Hess, M.D., to invent electronic fetal heart rate monitoring at Yale in the 1960s. Born in China to Australian parents in 1917, he grew up in Australia and came to the United States in 1945 to attend Loma Linda Medical School, then known as the college of Medical Evangelists of the Seventh-Day Adventist Church. Hon and Hess published their landmark paper on fetal electrocardiography in Science in 1957. Hon received numerous awards, including the Distinguished Service Award of the American College of Obstetricians and Gynecologists.

Robert F. Hustead, M.D. '54, died on December 6 from complications of pneumonia in Baltimore, Md. He was 80. Hustead was a longtime resident of Wichita, Kan., and a world-renowned anesthesiologist. From 1957 to 1959 he was a captain in the U.S. Army and served at the Edgewood **Chemical Biological Center in** Aberdeen, Md. In 1959 he became an instructor in anesthesiology at Johns Hopkins University School of Medicine, where he started the anesthesiology department. In 1961 he moved to Kansas City to take a position as assistant professor at the University of Kansas School of Medicine. He patented numerous medical

devices and invented the Hustead epidural needle, used to eliminate childbirth pain.

W. Raymond James, M.D. '44, died on December 16 at his home in Essex, Conn. He was 89. After an internship in Los Angeles and a residency at Columbia Presbyterian Hospital in New York, James and his wife moved to Essex in 1948, where he practiced medicine. A proponent of regionalization and special education, he served on the Essex Board of Education and the Region 4 Board of Education. He was also a health officer in area towns and won awards for his efforts to clean up the polluted lower Connecticut River.

Mildred H. January, M.D. '35, died on January 5 in West Hartford, Conn., after a long period of failing health. She was 101. After postgraduate training January specialized in psychiatry and psychoanalysis. She maintained a private practice in Hartford, Conn., and was affiliated with clinical settings in Stamford, New Britain, New Haven and Hartford.

Edward M. Kenny, M.P.H. '63, died on November 26 of prostate cancer. He was 78. Kenny was the assistant administrator at Stamford Hospital from 1963 to 1965; assistant administrator at Manchester Memorial Hospital from 1965 to 1967; executive director of Manchester Memorial Hospital from 1967 to 1983; and president and CEO of the Greenwich Hospital Association from 1984 to 1991. He served for more than two decades in the U.S. Army Medical Service Corps and retired with the rank of lieutenant colonel in 1979. He was a recipient of the **Connecticut Hospital Association**



T. Stewart Hamilton, M.D., Annual Award for Distinguished Service and was a member of the boards of Workers' Compensation Trust, Opportunity House (for autistic residents) and Milford Hospital.

James M. Lansche, M.D., HS '53. died on November 2 in Pocatello, Idaho, He was 78, Lansche became the first neurosurgeon in Pocatello when he moved there from California in 1972. He was chief of staff at the Bannock Regional Medical Center and served on several professional boards, including the State Board of Medical Discipline, as well as in numerous civic and professional organizations. After retiring in 1992, he spent much of the year at his cabin on Henry's Fork of the Snake River.

Anthony Lovell, M.D. '67, died on November 15 at his home in Springfield, Mass., of a glioblastoma. He was 68. Lovell had recently retired after 35 years as a cardiologist in Springfield. The son of a lobsterman on Cape Cod, Lovell earned money for college and medical school by shell fishing and commercial fishing. Long interested in serving the community, he helped initiate one of the region's first cardiac rehabilitation programs at the Springfield YMCA.

John L. Mahoney, M.D. '63, HS '69, died on October 5 of prostate cancer at his home in Oakland, Calif. He was 71. After an internship at Seton Hall University Medical Center in New Jersey, Mahoney joined the U.S. Marine Corps as a captain and instructor in neuropsychiatry. In 1973 Mahoney took a position as staff psychiatrist at Highland General Hospital in Oakland. He also started a private practice, consulted at senior living centers and in 1999 became staff psychiatrist at San Quentin State Prison. In 2004 he transferred to Solano State Prison. He retired in 2006.

Hugh J. McLane, M.D. '46, died at his home in the Laurel Lake Retirement Community in Hudson, Ohio, on January 11. He was 85. After attending Amherst College and the School of Medicine, McLane served in the U.S. Army Medical Corps in Berlin from 1947 to 1949. He completed his residency in internal medicine at Henry Ford Hospital in Detroit. He practiced internal medicine in Fond du Lac, Wis., for more than 40 years and retired in 1992. He served as president of the Fond du Lac Medical Society and president of the Wisconsin Heart Association.

Allan R. Oseroff, M.D. '76, PH.D., died on October 16 in Buffalo, N.Y. He was 65. Oseroff was chair of dermatology at the University of Buffalo and at the Roswell Park Cancer Institute in Buffalo. He was internationally recognized for the photodynamic treatment of skin cancer.

Frederic M. Richards, PH.D., a structural biologist and an innovative leader in the study of the relationships between protein structures and their biological functions, died of natural causes at his home in Guilford, Conn., on January 11. He was 83.

Richards, professor emeritus of molecular biophysics and biochemistry, was instrumental in the development of molecular biophysics and structural biology at Yale and nationwide. His most paradigm-shifting experiment, published in 1958, provided the first evidence that a protein peptide's ability to form a three-dimensional structure is an intrinsic property of its amino acid sequence.

Richards obtained his PH.D. at Harvard in 1952. He pursued postdoctoral research at the Carlsberg laboratory in Copenhagen, Denmark, and at Cambridge University in England. In 1955 he joined the biochemistry faculty at Yale and in 1963 merged the departments of biochemistry and biophysics to form the Department of Molecular Biophysics and Biochemistry, with a mandate to move the department into the new field of molecular biology. Between 1963 and 1967 and from 1969 to 1973, as chair of this new department, Richards initiated the development of one of the major centers in the world for the study of biophysics and structural biology.

Richards was a member of the National Academy of Sciences the American Academy of Arts and Sciences, and the American Philosophical Society. He was awarded the Connecticut Medal of Science in 1995.

Samuel Ritvo, M.D. '42, a faculty member at the Yale Child Study Center for nearly six decades, died on December 3 while hospitalized for treatment of lymphoma in Maryland. He was 91. Ritvo graduated from Harvard College in 1938. He trained in pediatrics at the University of Minnesota and in pediatrics and psychiatry at Columbia University in New York. He joined the Yale faculty in 1950 as part of the reorganization of what became the Child Study Center and held the rank of clinical professor of psychiatry from 1965 until his retirement in 2007. The first director of training in child psychiatry at Yale, Ritvo was a training and supervising analyst at the

New York Psychoanalytic Institute and the Western New England Institute of Psychoanalysis in New Haven. A highly respected teacher and clinician, Ritvo trained generations of child psychiatrists.

Jerome H. Shapiro, M.D. '48, died on October 14 in Bedford, Mass.. from complications of Alzheimer disease. He was 84. Shapiro served in the U.S. Army during World War II and completed his medical education following his discharge. He was president of the Massachusetts Radiological Society, the New England Roentgen Ray Society and the American College of Radiology (ACR). He received the ACR gold medal in 1992 and a gold medal from the Radiological Society of North America in 1996.

Ellis J. Van Slyck, M.D. '47, died on December 20 in Grosse Pointe, Mich. He was 84. After his residency and service in the U.S. Army Medical Corps during the Korean War, Van Slyck joined the hematology division at Henry Ford Hospital in Detroit. He authored or co-authored 80 publications about his specialty, cancer and hematologic disorders. From 1981 to 1983 he chaired the medical advisory board of The Children's Leukemia Foundation of Michigan.

SEND OBITUARY NOTICES TO Claire M. Bessinger, Yale Medicine, 300 George Street, Suite 773, New Haven, CT 06511, or via e-mail to claire.bessinger@yale.edu



A student-run free clinic grows and thrives

The idea was simple—free primary health care for the uninsured. Five years ago students in medicine, nursing and public health and in the Physician Associate Program opened the HAVEN Free Clinic in partnership with the Fair Haven Community Health Center (FHCHC). [See "Students Reach Out to the Uninsured at Free Medical Clinic in Fair Haven," *Yale Medicine*, Autumn 2006.] Supervised by faculty from the schools of medicine and nursing, the students saw three or four patients a week. Now HAVEN serves more than 20 patients a week during its Saturday morning hours. Unlike the FHCHC, which has a sliding scale, HAVEN does not charge for its services or for medications.

Since its beginnings five years ago, the student-run clinic has added services to meet the needs of its growing patient population, said Susan Mathai, a fourth-year medical student and one of HAVEN's directors. In response to student observations of unmet mental health needs among female patients, a support and educational group for women has been started. A new program for latent tuberculosis patients is improving medication adherence. HAVEN's expanded capacity and services have been made possible by a variety of gifts and grants from members and friends of the medical school community and such philanthropic organizations as the Community Foundation for Greater New Haven and the Gilead Foundation.

Along with more services have come more opportunities for students to learn about the challenges of caring for lowincome patients. HAVEN has drawn on the FHCHC professional staff, volunteers from the medical school community and fulltime faculty members to serve as attending physicians. According to Frederick Haeseler, M.D., associate clinical professor of medicine and HAVEN's medical student advisor, faculty volunteers value the opportunity to teach committed students and help care for patients in need.

"A lot of good things are possible," said Mathai. —*Colleen Shaddox*

Archives 50 AND 25 YEARS AGO



Alumni Day 1959 —Alumni Bulletin May 1959

"Those who attended the February Alumni Day activities at the School of Medicine were privileged to hear a stimulating panel discussion on 'Recent Advances in Cardiovascular Surgery at Yale.' This program was arranged and moderated by Dr. William W.L. Glenn, associate director of surgery, who heads the section of cardiovascular surgery. ...

"The growth of cardiovascular surgery at Yale has been possible through the integrated efforts and cooperation of various departments in the School of Medicine, and it was not possible to include all who have been active in this important field. ...

"Recent advances in the diagnosis of heart disease in the adult were reviewed by Dr. Allan V.N. Goodyer ('42), associate professor of medicine, who heads the cardiovascular section of the Department of Medicine. He was followed by Dr. Richard L. Barach ('49), assistant professor of radiology, who presented a remarkable motion picture taken during fluoroscopy to illustrate cineangiography in the diagnosis of congenital heart disease. Features of various anomalies amenable to right heart bypass were discussed by Dr. Marie J. Browne, clinical fellow in rheumatic fever and heart disease, of the Department of Pediatrics.

"In conclusion, Dr. Glenn contributed some observations on the breadth and scope of cardiac surgery. A pump oxygenator (heartlung machine) currently being used in open heart surgery was demonstrated. As a special bonus, Dr. Alexander Mauro, assistant professor of physiology, was called upon to describe a newly developed electronic cardiac pacemaker. ... which recently under went its first clinical trial successfully."



... In Progress: Cancel —Yale Medicine Summer/Fall 1984

"The National Cancer Institute recently awarded a grant of \$421,000 for support for three years of research being conduct by Dr. Sara Rockwell on the use of perfluorochemical emulsions as adjuncts to radiotherapy. The target for this research is impro treatment of those solid tumor: which are resistant even to the of current treatment. ...

"In preliminary studies, Dr. Rockwell and her colleagues hav found that infusing laboratory animals that have breast cancer sarcomas with Fluosol and havin them breathe oxygen before and during radiotherapy increases th number of tumor cells killed b radiation, but does not increas the toxicity of the radiation to th blood-forming cells of bone mar row. Further studies will examine the effect of Fluosol treatment d other tumors and other normal t sues, to evaluate whether this a in combination with radiotherap has the potential for effective tr ment of solid tumors in humans




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BICENTENNIAL SURVEY CHARLES GERSHMAN INSTITUTIONAL PLANNING & COMMUNICATIONS YALE SCHOOL OF MEDICINE PO BOX 208331 NEW HAVEN CT 06520-9917 **FROM A DONOR IN THE ANATOMY LAB, A FINAL LESSON** Four first-year medical students in the anatomy lab watched closely in February as Shukrulla Ghofrany, M.D., lecturer in surgery (gross anatomy), hunted for the .22-caliber bullet in the body of the donor they'd been studying since the fall. An X-ray showed that it was lodged near the 12th vertebra, and Ghofrany was struggling to find the shell, which had gone untouched for 73 years.

"The bullet is intact, so we know it didn't hit bone," said William B. Stewart, Рн.д., chief of the section of anatomy and experimental surgery, as he studied the X-ray.

While Ghofrany probed, student Rany Woo methodically kneaded the donor's kidney. "What's that?" she asked. Moments later, she held the bullet in her gloved hand as classmates crowded around.

The students couldn't have known it, but the man who donated his body after learning he had incurable lymphoma would have taken great satisfaction from this scene. C. Charles Peterson, "Chuck" to family and friends, "loved to teach," said his widow, Carolyn.

Peterson was 7 years old when his playmate accidentally shot him with a gun the boys had found in a neighbor's bedroom. The doctors left the bullet because Peterson was unbothered by it.

Peterson lived a full life until his death in December 2007 at the age of 80. He married and had five children, served in the Naval Air Corps as a night carrier pilot, initiated an after-school computer program while teaching in Missouri in the 1960s, wrote and taught a hands-on science program for the American Association for the Advancement of Science, and was vice president of Middle East programs for Sikorsky Aircraft.

Peterson shared his wish to donate his body with his family, who, after some agonizing, agreed. "Dad was a teacher and a scientist, and furthermore, he loved to work," son Charles said. "This is the very thing he'd want, that after he died, he'd have a job to do."

—Jennifer Kaylin



First-year medical students Josh Au, Chineme Enyioha, Rany Woo and Kenneth Ike examined the .22-caliber bullet they found in the body of their anatomy lab donor. The donor had been shot accidentally by a playmate 73 years earlier, but the bullet was never removed.

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 An evening with Richard A. Silverman, Director of Admissions MK The Restaurant, 868 North Franklin, Chicago

1999

Silverman

2004







