

Yale Medicine

spring 2006

Six Yale faculty
named to IOM

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Yale connections
around the world

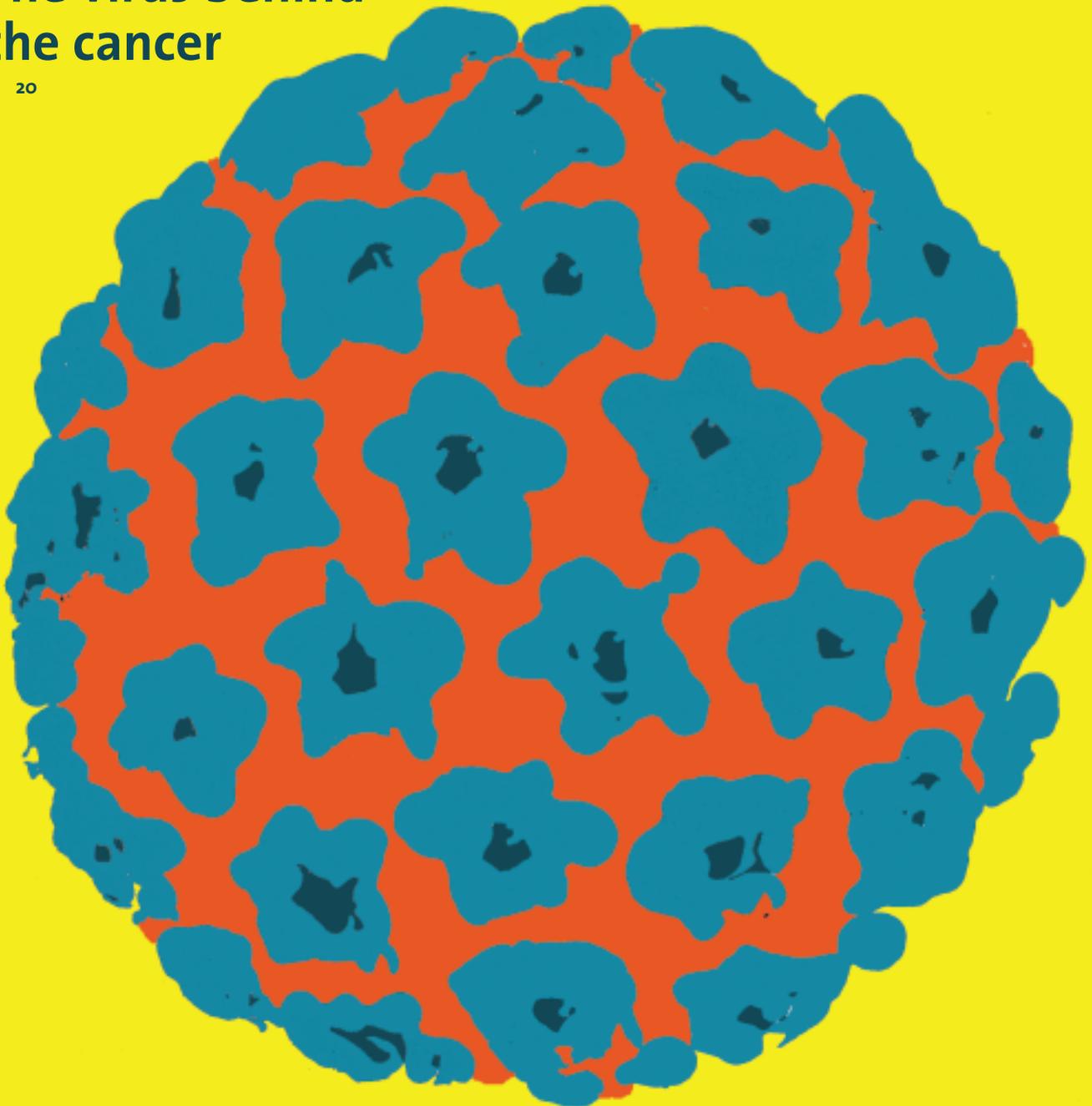
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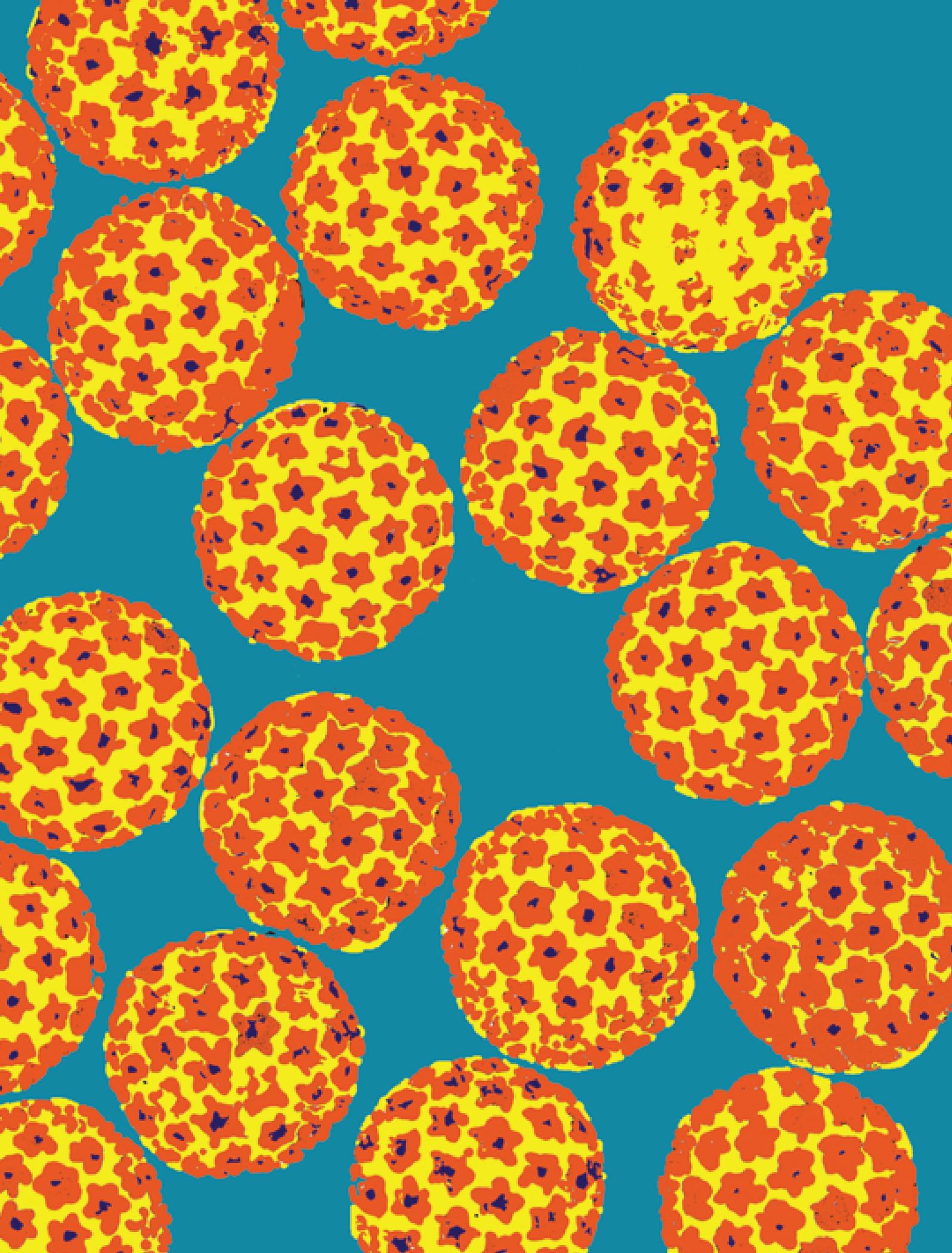
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SPRING 2006

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yalemedicine.yale.edu

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

ON THE COVER

The human papillomavirus (HPV) is a common infection spread through sex and skin-to-skin contact. Since 1975 it has been linked to cervical cancer.

BACKGROUND

HPV has helped scientists understand how a virus can lead to cancer. It is a member of a family of small DNA viruses that typically cause benign warts. But some high-risk HPV types have been linked to carcinomas, including cervical cancer. The virus is also thought to play a role in other anogenital cancers, skin cancers and some head and neck tumors.

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HOW TO REACH US

Yale Medicine welcomes news and commentary. Please send letters to the editor (350 words or less) and news items to *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612, or via electronic mail to yymm@yale.edu, and include a daytime telephone number. Submissions may be edited for length, style and content.

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yalemedicine.yale.edu

News of my demise is premature

According to the alumni reunion report for the Class of 1960 published in the Autumn 2005 issue of *Yale Medicine*, Jerrold M. Post, M.D. '60, led the class in "a brief silence in honor of our deceased classmates," including me. While I am deeply honored, I am completely undeserving.

My wife, Rosemary, died three years ago. I am running an active research program at the University of Connecticut Health Center. I have participated in the Class of 1959 reunions, since I was closer to them, having taken a year off after the third year to do research before graduating.

*D. Kent Morest, M.D. '60
West Simsbury, Conn.*

Dishonest reporting in Vietnam and PTSD

As a combat surgeon in DaNang in 1968, I experienced the Tet Offensive firsthand and saw more carnage than most civilian surgeons see in a lifetime. Cathy Shufro's "The Unseen Wounds of War" [Autumn 2005] brings back memories—and prompts a few questions.

Dishonest media coverage of Vietnam, specifically the reporting of the Tet Offensive as a defeat of our forces, was the reason our veterans returned to a hostile public.

Did any of Ms. Shufro's vets mention that our forces never lost a significant battle in Vietnam? Did Ms. Shufro run across data showing that victorious combatants who return to be hailed as heroes suffer less post-traumatic stress disorder than do defeated forces? Could the confusion of returning to be spat upon and subjected to the disrespect and dishonor ordinarily reserved for the vanquished—*after defeating the enemy decisively in every encounter*—be a factor in the symptoms experienced by those in Ms. Shufro's group?

*Martin L Fackler, M.D. '59
Retired Col.,
U.S. Army Medical Corps
Gainesville, Fla.*

Chase leaving to study what makes good doctors

In December the medical school's deputy dean for education, Herbert S. Chase Jr., M.D., announced that he would be ending his six-year tenure at the end of the academic year on June 30. Chase will return to Columbia University's College of Physicians and Surgeons, where he spent 22 years before coming to Yale, to continue his research into the kind of teaching that makes a good doctor. "I am interested in looking at physician performance and patient outcomes, and asking whether and how one's medical educational background influences the quality of a physician's performance," Chase said.

Recruited in 1999, Chase was asked to evaluate the medical school curriculum and recommend and implement changes necessary to meet the challenges of a new landscape in medicine. He championed the merging of courses in related disciplines and encouraged a more fluid curriculum that would integrate the basic and clinical sciences over four years of study. As deputy dean he oversaw the revamping of the anatomy course for first-year students; the creation of the Society of Distinguished Teachers to reward outstanding faculty; and the implementation of the Clinical Skills Program, which provides rigorous instruction and assessment during the first two years of medical school. According to Dean Robert J. Alpern, M.D., "Yale has benefited greatly from [Chase's] commitment, enthusiasm and dedication to the medical students, and we take great pride in Herb's accomplishments as deputy dean."

Chase said that credit for his achievements is not his alone. "Whatever was accomplished, was accomplished with great effort by dozens of faculty."

—John Curtis

yale medicine

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A world of connections

This issue's feature lineup begins with a tale of connections—among Yale alumni and faculty, among doctors and patients and among old school friends. As related by Jill Max, these connections made it possible for a Yale medical student to do research in Italy, and also for her mother in Serbia to receive a critical, life-changing procedure.

For our cover story, “The Virus Behind the Cancer,” Contributing Editor Jennifer Kaylin looks at a different type of connection. She traces the guesses, speculation and discoveries that led scientists to the viruses that underpin about 10 percent of all cancers. Those connections between viruses and cancer could yield clues that will put scientists on the path to vaccines and treatments.

Contributing Editor Marc Wortman donned a jumpsuit and entered the pathology labs to observe an autopsy for his article, “The Final Chapter.” Wortman examines why autopsies are so rarely done, even though it is through the autopsy that all of the patient's medical history is connected in the last, most complete picture of his or her health.

Finally, in “When Animals Sound a Warning,” Rhea Hirshman explores the connections between human disease and the environment. Her research took her back to Captain Cook's discovery of Hawaii and the first Italian invasion of Ethiopia. In both instances new creatures introduced new

diseases, forever altering the ecology and epidemiology of those lands. That interaction is the focus of Yale's new Center for EcoEpidemiology, which brings together scientists in both fields.

In the spring of 2004 we asked Amelia Shaw, M.P.H. '03, who was in Haiti on a Fulbright Scholarship and making a documentary film about AIDS, to write about her experiences. Shaw cautioned us that although she'd interned at National Public Radio, she'd never written a feature-length magazine article. Her first drafts convinced us we'd made the right choice. Shaw's passion and commitment infused every page of her story [“A Film to Finish,” Fall/Winter 2004].

This spring the Association of American Medical College's Group on Institutional Advancement seconded our opinion by honoring Shaw with a Robert G. Fenley Writing Award of Excellence for her article. The award, given annually, recognizes outstanding writing. We couldn't agree more. Congratulations, Amelia.

John Curtis
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SECOND OPINION BY SIDNEY HARRIS



“APPARENTLY, MR. FIADKIN, EVOLUTION IS
 A TWO-WAY STREET.”



TERRY DAGRADI

The Institute of Medicine elected a record number of Yale scientists to its ranks last year. From left, Pietro De Camilli, Gerald Shulman, Joan Steitz, Kelly Brownell, Margaret Grey and Joseph Schlessinger, joined by Carolyn Slayman and Dean Robert Alpern.

Six at Yale named to Institute of Medicine

Top honor goes to experts in drug development, diabetes, obesity, neuroscience and genetics.

Six Yale researchers, five from the School of Medicine and one from the School of Nursing, were elected to the Institute of Medicine (IOM) of the National Academies in October. Their election brings the number of Yale scholars in the IOM to 37, including two at the School of Management and one at Yale-New Haven Hospital.

"It is unprecedented in recent memory that so many from our institution have been elected in a single year," said Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. Previously, according to IOM records, no more than three Yale scientists had been elected in one year. These elections, Alpern said, give Yale one of the highest concentrations of members of any institution in the nation.

The six were honored at a reception in the Medical Historical Library in December.

Elected this year are Kelly D. Brownell, PH.D., chair and professor of psychology, professor of epidemiology and director of the Rudd Center for Food Policy & Obesity; Pietro De Camilli, M.D., FW '79, the Eugene Higgins Professor of Cell Biology and a Howard Hughes Medical Institute investigator; Margaret Grey, R.N., DR.PH., the Annie Goodrich Professor of Nursing and dean of the School of Nursing; Joseph Schlessinger, PH.D., the William H. Prusoff Professor of Pharmacology and chair of pharmacol-

ogy; Gerald I. Shulman, M.D., PH.D., professor of medicine and of cellular and molecular physiology and a Howard Hughes Medical Institute investigator; and Joan A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry.

Brownell is perhaps best known for his efforts to curb obesity, which form part of his studies of the intersections of behavior, environment and health. De Camilli is a cell biologist interested in understanding molecular mechanisms in presynaptic function and the role of phosphoinositide metabolism in the regulation of membrane traffic. Schlessinger's lab studies the mode of action of growth factor receptors and the intracellular signaling pathways that are activated by growth factor stimulation. Shulman is an expert on the mechanisms of insulin resistance, the role of the liver and muscle in the pathogenesis of type 2 diabetes and the benefits of exercise in diabetes management. Steitz discovered snRNPs, small particles in cells that are necessary to convert genetic information into active proteins. Grey is renowned for her studies of adaptation to chronic illness in childhood, particularly in children with type 1 diabetes mellitus.

The Yale researchers are among 64 new members elected to the IOM in 2005. The IOM was established in 1970 by the National Academy of Sciences to honor professional achievement in the health sciences and to serve as a national resource for independent analysis and recommendations on issues related to medicine, biomedical sciences and health.

—John Curtis

A son of Yale and the medical school receives AYA's highest honor

At the end of World War II, Nicholas P.R. Spinelli, M.D. '44, took leave from his Army unit in Germany and hitched a ride on a cargo plane to Rome. From there he traveled to Faeto, a village in southern Italy overlooking the Adriatic Sea that his parents had left 30 years earlier, where the villagers celebrated the arrival of their native son. "I was there for three nights," Spinelli said. "I had to make rounds and visit every sick person in the village."

His triumphant return to his family's ancestral community was the result of his parents' belief in education and Spinelli's own belief in the value of his education at Yale, where he earned his undergraduate and medical degrees. Had they stayed in Italy, Spinelli said, his parents would never have been able to educate their yet-unborn children, Nicholas and his sister, Viola, M.P.H. '65. "Education was a passion with both my parents. That was why they were working so hard," he said.

Throughout his career Spinelli has shown his loyalty to Yale by raising money for the school, establishing with his classmates a scholarship fund, serving as the medical school's director of alumni affairs and sponsoring the first White Coat ceremony in 1992.

In November the Association of Yale Alumni awarded Spinelli the Yale Medal, which, since 1952, has honored outstanding service to the university. In this recognition, Spinelli joins such other medical school graduates and faculty as pediatrician Grover F. Powers, M.D.; Russell B. Scobie, M.D. '29; William L. Kissick, M.D. '57, M.P.H. '59, DR.PH. '61; Muriel D. Wolf, M.D. '59, HS '60; and the legendary Dean Milton C. Winternitz, M.D.

Spinelli's path to Yale began in Stratford, Conn., where his parents had settled. His father ran a succession of businesses, including a gas station

and restaurant on the Boston Post Road, the main thoroughfare between New York and Boston.

In 1937 Spinelli entered Yale College, planning to become a writer. At the end of his freshman year, however, he took a job in a biology laboratory, where a professor encouraged him to study medicine, and in the fall of 1941 he entered the School of Medicine.

A few months later, while preparing for an anatomy exam, he heard President Roosevelt announce on the radio that the nation was at war. Spinelli and his 42 classmates were inducted into the Army, and their medical education was accelerated to meet wartime needs. Upon his discharge Spinelli returned to Stratford to practice internal medicine. A heart attack forced his retirement in 1958, but he began a second career as director of medical education at Bridgeport Hospital. In the 1980s his second career gave way to a third career as director of alumni affairs at the medical school. His main concern there was what he called "incubating alumni," strengthening relations with students and bringing them into the fold by including them in alumni events. At that time he helped create the Committee on the Well-Being of Students, which makes a report each year on issues of concern to students.

Perhaps his greatest gift to the medical school was his proposal to his classmates at their 40th reunion in 1984. He asked them to contribute to a scholarship fund over the next decade. By then, he said, the fund would be large enough to offer its first scholarship. In 1994, with 100 percent participation from the class, the fund paid half the expenses of a first-year student. Eleven years later the fund was supporting up to three students through their first year.

"I have gotten letters from students who have been given the scholarship, saying how important it was and how they couldn't have gone to medical school without it," Spinelli said.



For his long-standing service to the university and the School of Medicine, Nicholas Spinelli received the Yale Medal from the Association of Yale Alumni. At the ceremony in November Spinelli signed the President's Book.

For his service to Yale, Spinelli received the Distinguished Alumni Service Award from the Association of Yale Alumni in Medicine in 1987 and the Peter Parker Medal in 1994. In recognition of his contributions to the medical school, two rooms were named in Spinelli's honor in 2000, the medical school's Office of Alumni Affairs and one at the Center for Neuroscience and Regeneration Research at the VA Connecticut Healthcare System in West Haven.

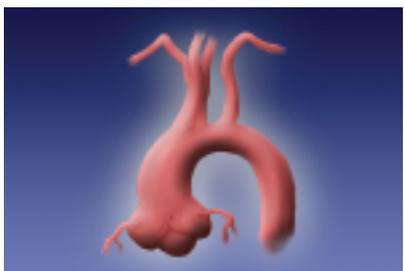
But no honor, he said, surpasses the first he received from the university when he was 16 years old. "The greatest gift I got was the letter saying I was accepted to Yale."

—J.C.

From Student Research Day to a scholarly publication and *The Wall Street Journal*

Last May at Student Research Day, Hardean Achneck, M.D. '05, described a link between atherosclerosis and aortic aneurysms. The aneurysms, he found, seemed to protect against atherosclerosis, a deadly form of arteriosclerosis.

By summer's end Achneck's research was published in the journal *Chest* and reported in *The Wall Street Journal*. Achneck was first author of the journal paper; the senior author was his advisor, John A. Elefteriades, M.D. '76, HS '81, FW '83, professor and chief of cardiothoracic surgery. "I am very happy to see the results become so well-received," said Achneck, now



Yale researchers believe that aortic aneurysms, such as the annuloaortic ectasia aneurysm shown above, protect against atherosclerosis.

a surgical resident at Duke University School of Medicine.

The research began years ago and arose from repeated observations in the operating room. "Operating every day we noticed that in patients with aneurysms at the top of the chest, their arteries were pristine," said Elefteriades. "They were like babies' arteries, teenagers' arteries." Typically, he said, even men in their early 20s have fatty streaks and plaque in their arteries.

Elefteriades has long welcomed medical students working on their theses, and he first assigned this project to Biren P. Modi, M.D. '02. With the research still ongoing when Modi graduated, Achneck picked up the project and spent a fifth year at Yale working on it.

Literature searches, he said, yielded no articles exploring the links between two types of aneurysms located in the ascending aorta—annuloaortic ectasia and type A dissection—and atherosclerosis. The next step was to find 64 patients with both types of aneurysm, and a control group of 84 patients with no history of aneurysms. The control patients came from the emergency department, where they had received treatment for trauma and had had CT scans of their chests.

The patients who had aneurysms, the study found, were less likely to have atherosclerosis. This was independent of all common risk factors for atherosclerosis. "It was a statistically powerful finding," Elefteriades said, adding that it fits with the results of laboratory research. "There are some strains of rodents that have been developed that are prone to aneurysms, and they are protected from arteriosclerosis."

Why and how aneurysms offer protection from atherosclerosis remains unclear. Elefteriades and his colleagues are looking at enzymes called matrix metalloproteases (MMPs), which degrade material that accumulates on arterial walls. "It may be, and this is not proven," said Achneck, "that some of these MMPs are causing aneurysms on the one hand and chewing up atherosclerosis on the other.

The gene for MMP3 is on a section of chromosome 11 that is known to cause mutations that increase the risk of aortic aneurysms. Elefteriades and colleagues are working with Celera Diagnostics to explore the underlying genetics.

Since his graduation Achneck has been focusing on his residency. "I'm trying to survive," he said.

—John Curtis

KESSLER PORTRAIT UNVEILED

David A. Kessler, M.D., former dean of the medical school, returned to the Sterling Hall of Medicine in December for the unveiling of his official portrait by artist Richard Whitney. At a ceremony in the Historical Library, colleagues and Yale President Richard C. Levin lauded the achievements of Kessler's tenure from 1997 to 2003, specifically the construction of the Anlyan Center for Medical Research and Education and the recruitment of 11 department chairs. Kessler said that although the portrait is of one person, many people contributed to his accomplishments as dean. "These things do not happen alone," he said.





New five-year public health program gives undergrads a head start

Yale junior Sarah Milby has always been interested in pursuing a career in public health and community development, and a new joint-degree program may be able to give her a head start. Milby, a premed and history of science/medicine major, plans on being one of the first applicants to a new five-year joint-degree program that will allow her to earn a B.A. or B.S. at Yale College and an M.P.H. from the Yale School of Public Health (EPH). "I'm so excited to start preparing for my career in public health as a senior," she said.

The program is designed to give students a broad understanding of the factors that shape public health and to equip them with the tools necessary to address public health issues, such as the fight against chronic disease and the impact of environmental stressors on human health. It is open to all undergraduates, regardless of their major. Students would normally apply to EPH during the spring of their sophomore year, but juniors may also apply this spring, when the first wave of applications will be considered.

Developed over the past two years, the program is a response to increasing student interest in the field of public health and serves as an alternative to the two-year master's program already in place. "There has been evident a very large demand on the part of undergraduates, who are agitating for more course experiences and educational opportunities that allow them to take their classroom knowledge and put it into more concrete and applied

settings," said Mark J. Schlesinger, PH.D., director of undergraduate studies at EPH and professor in the Division of Health Policy and Administration. He also views the program as an opportunity for EPH to connect itself more extensively with Yale College.

In addition to completing the requirements for their undergraduate major, students in the new program will complete six public health courses, such as health policy, biostatistics and principles of epidemiology, during their junior and senior years. Between the fourth and fifth year they will complete a public health internship, and during the fifth year they will be enrolled full-time at EPH in one of the school's eight divisions, where they will complete 10 courses and a master's thesis.

The five-year program and a new one-year mid-career program for health care professionals will bring both older and younger students to EPH. "Each group will bring its own distinctive resources into the classroom," said Schlesinger. "I think it will make the classroom experience much richer for all the students."

For undergrads who are anxious to begin earning a graduate degree in public health while working toward their bachelor's degree, the combined program is a welcome addition. "I want to start my life and make a difference," said Milby. "That's why this is just too good to be true."

—Jill Max

et cetera ...

GERMAN PHARMA FUNDS RESEARCH

The School of Medicine and Boehringer Ingelheim Pharmaceuticals Inc. (BIPi), the Ridgefield, Conn.-based division of the German pharmaceutical firm, have formed an alliance to explore treatments for cardiovascular, inflammatory and autoimmune diseases. Under the agreement, formalized last July, BIPi will fund research projects at Yale, several of which are already under way. The projects are investigating the role of inflammation in organ rejection and atherosclerosis; channels that admit calcium into immune system cells; enzymes that act in the kidneys to regulate salt and fluid balance; and the formation of new blood vessels in the heart.

"Yale, with its excellence in immunology and cardiovascular research, offers a real opportunity for mutual benefit," said Mikael Dolsten, M.D., PH.D., head of corporate division pharma research at BIPi's world headquarters in Ingelheim, Germany.

BIPi will work with scientists in the Section of Immunobiology and in the Interdepartmental Program in Vascular Biology and Transplantation.

—Peter Farley

BRAIN DATA ON THE INTERNET

In an effort to help neuroscientists quickly find the latest information about the brain, the National Institutes of Health has established a consortium to design a Neuroscience Information Framework (NIF). The consortium includes scientists at Yale, the California Institute of Technology, Weill Medical College of Cornell University, George Mason University and the University of California at San Diego.

The NIF will help guide scientists to resources on the Internet by identifying software tools and data, developing language to describe the resources and placing them in a Web-accessible database. "To use this information effectively, neuroscientists need to be able to locate the latest research results that are relevant to the particular behavior they are studying or neurological disease they are treating," said Gordon M. Shepherd, M.D., PH.D., professor of neuroscience and neurobiology and a member of the Yale team.

—J.C.

How to fix the broken telephone

Phone conversations are a major source of miscommunication between doctor and patient.

As soon as the words were out of her mouth, she regretted them: while returning phone calls for a colleague, Anna B. Reisman, M.D., assistant professor of medicine, told the woman who answered the call that her husband had tested positive for gonorrhea. Not only should Reisman have declined to share test results with a family member, but as it turned out, she had misread the patient's chart. The family accepted Reisman's apology, but she'll never forget her indiscretion, and in the seven years that have passed

she's often asked herself how it could have been avoided.

Communication failures have been shown to play a key role in medical mishaps; telephone encounters, which account for 25 percent of interactions between physicians and patients, are particularly tricky. There are no visual cues to tell the physician how the patient is feeling, how he or she is reacting to a diagnosis or whether the patient can speak freely—all of which can set the stage for preventable errors.

In a paper published in the October issue of the *Journal of General Internal Medicine*, Reisman and co-author Karen E. Brown, M.D., assistant professor of medicine, outlined scenarios in which communication errors commonly occur, providing strategies to minimize mistakes. The scenarios involve sensitive test results, requests for narcotics, patients who are unwell but not sick enough for the emergency room, late-night calls, communicating with unintelligible patients and calls from patients' family members. In one scenario, a patient calls his physician in the middle of the night with back pain. Irritated at being awakened for a seemingly petty concern, the doctor terminates the call before the patient can explain that his symptoms include chest pain; the patient ends up hospitalized with a mild heart attack. In this situation, Reisman and Brown discuss the importance of careful questioning and suggest ways of drawing out hidden concerns. They advise giving the patient time to describe the chief complaint before interrupting, asking the patient why he or she is calling at that time and finding out if there is anything else the patient wants to commu-

nicate. In another scenario regarding sensitive test results, the strategies include scheduling an office visit (which can later be cancelled) when ordering tests that might have significant results; ensuring that patients can speak freely if the test findings are given over the phone; and not leaving results with family members or recorded on an answering machine. (Since the passage of the Health Insurance Portability and Accountability Act in 1996, all hospital staff have received training in protecting patient confidentiality.)

Physicians assess patients by observing aspects of their appearance, but the opportunity for visual inspection is missing in phone encounters. Improving phone skills can help doctors fill in some of that information. "Better communication improves doctor-patient relationships, decreases lawsuits and improves outcomes," said Reisman.

Despite advances in other communication technologies, the telephone will continue to play a major role in doctor-patient relationships, yet according to a 1995 survey, telephone medicine is taught in only 6 percent of residency programs. Reisman began teaching it to residents and physicians when she noticed how frequently residents talked about mistakes they had made when dealing with patients over the phone. By teaching the best way to handle telephone encounters, she hopes to help others avoid mistakes similar to the one she made almost a decade ago.

(For a different view of the clinical use of phones, see "Cell Phones Reduce Errors" on the next page.)

—Jill Max



et cetera ...

Study finds sleep apnea is a major risk factor for stroke and death

Although previous studies have suggested links between sleep apnea and stroke, it was never clear whether the increased risk of stroke was related to such other factors as hypertension or diabetes. Now, in a study published in *The New England Journal of Medicine* in November, a Yale team has found that, regardless of other factors, sleep apnea can put people at risk for stroke—the third leading cause of death in the developed world.

“Our study shows that sleep apnea doubles the risk for development of stroke and death, and severe sleep apnea more than triples the risk,” said H. Klar Yaggi, M.D., assistant professor of medicine and principal investigator of the study. “We know that this risk was independent of other risk factors, including high blood pressure.”

As many as one in five adults in the United States suffer from sleep apnea, which causes them to stop breathing temporarily while they sleep. Their bed partners may notice such symptoms as loud snoring, gasping or pauses in breathing. Men are more at risk for sleep apnea than women; obesity is also a risk factor.

The new study, conducted between January 1997 and December 2003, enrolled 1,022 patients over the age of 50 who had gone to the Yale Center for Sleep Medicine for treatment. About 68 percent, 697 patients, had been diagnosed with obstructive sleep apnea syndrome. Hypertension, diabetes and obesity were more prevalent in this group. The mean apnea-hypopnea



Klar Yaggi found that sleep apnea doubles the risk for stroke and death and severe sleep apnea triples the risk.

index—the number of episodes of breathing cessation per hour—of those with the syndrome was 35. Those in a comparison group who did not have obstructive sleep apnea syndrome had a mean index of 2.

An unadjusted analysis found an association between obstructive sleep apnea syndrome and stroke or death from other causes. Age and diabetes, for example, were significant factors. But even after adjusting for age, sex, race, smoking, alcohol consumption and diabetes or cardiovascular disease, the study still found a significant link between sleep apnea and stroke or death. Only 16 in the comparison group suffered stroke or death, but 72 patients with obstructive sleep apnea syndrome had a stroke or died.

The study was supported by the National Institutes of Health, the Department of Veterans Affairs and the Yale Center for Sleep Medicine.

—John Curtis

PESTICIDE LINKED TO INFERTILITY

A common pesticide may interfere with the reproductive tract, leading to reduced fertility in women, according to Yale researchers.

In an article published in *Endocrinology* last August, the researchers reported that in studies in mice and in human tissue, methoxychlor (MXC), a substitute for the banned pesticide DDT, alters an estrogen-regulated gene in the reproductive tract and reduces the ability of the uterus to support embryo implantation. MXC, which is applied to crops, livestock, home gardens and pets, is one of several chemicals that can mimic the action of hormones and sometimes interfere with endocrine function.

“MXC has an adverse effect on these mice similar to that of DES, a synthetic estrogen,” said senior author Hugh S. Taylor, M.D., HS '92, associate professor in the Division of Reproductive Endocrinology and Infertility in the Department of Obstetrics, Gynecology and Reproductive Sciences. “Female offspring of women exposed to DES were more likely to have an abnormally shaped cervix and were more prone to cancer of the vagina, miscarriages, early labor and other complications.”

—J.C.

CELL PHONES REDUCE ERRORS

Cell phones have long been banished from hospitals over fears of interference with medical devices. A study by a Yale anesthesiologist and colleagues, however, suggests that mobile phones speed communications and reduce medical errors. And digital phones rarely cause interference.

For a study published in *Anesthesia & Analgesia* in February, Keith J. Ruskin, M.D., associate professor of anesthesiology and neurosurgery, surveyed attendees at the 2003 meeting of the American Society of Anesthesiologists. Based on more than 4,000 responses, Ruskin found that 65 percent of anesthesiologists relied on pagers to communicate and 17 percent used cell phones. Of those who used pagers, 45 percent reported delays in communications. Only 31 percent of those who relied on cell phones reported delays.

—J.C.



TERRY DAGRADI

In separate studies, Matthew State and Jeffrey Gruen discovered links among genetic mutations, brain development and disease.

Two Yale teams among *Science* Top 10 for 2005

Genetic mutations linked to brain development and disease were among last year's leading discoveries.

Two findings by Yale scientists have been included in *Science* magazine's list of the 10 leading scientific breakthroughs of 2005. The teams found evidence that both Tourette syndrome (TS) and dyslexia could stem from genetic defects linked to brain development. Their work was among research cited under the category "Miswiring the Brain." Although the article did not name specific scientists or institutions, it cited "clues about the mechanisms of diverse disorders including schizophrenia, Tourette syndrome, and dyslexia. A common theme seems to be emerging: Many of the genes involved appear to play a role in brain development."

Matthew W. State, M.D., Ph.D. '01, the Harris Assistant Professor of Child Psychiatry and assistant professor of genetics, and the senior author of a report in the October 14 issue of *Science*, led the team that identified for the first time a genetic mutation associated with TS. The gene, which contributes to neuronal growth and communication, accounts for less than 2 percent of TS cases, but its discovery after years of searching offers the best chance yet to penetrate this socially debilitating disease. How the mutations participate with other genetic and environmental factors to increase risk for the disease is unknown. "We hope the clues this gene will give us will have widespread ramifications for

understanding the basic biology of this disorder," said State.

In its search for "that one unusual patient who would lead us to a gene," State's team found a child, diagnosed with TS and attention deficit hyperactivity disorder, who had a telltale break on chromosome 13. That clue led researchers to the nearby *SLITRK1* (*Slit* and *Trk*-like family member 1) gene, which had already been recognized to be active in the developing brains of rodents and to function in neuron growth. When they analyzed the gene from 174 people with TS, they found three individuals with mutations. No mutations of any kind were found in several hundred unaffected people, providing strong evidence that *SLITRK1* was contributing to the disease. Studying *SLITRK1* gives a starting point, said State, who likened their discovery to a string the researchers can now pull on to start to unravel the rest of the disease.

Another team at the School of Medicine found a genetic link to dyslexia, the reading disorder that affects millions of children and adults. A mutated version of a gene, located on chromosome 6 and called *DCDC2*, disrupts the formation of brain circuits that make reading possible. The findings deepen the "understanding of how the reading process works on a molecular level," said Jeffrey R. Gruen, M.D., HS '84, FW '88, associate professor of pediatrics and lead author of the study published in a special issue of *Proceedings of the National Academy of Sciences* in November.

In a study of DNA markers in 153 dyslexic families, Gruen's team found that up to 20 percent of cases of dyslexia are due to defects in the *DCDC2* gene. In the mutated version of the gene, a large regulatory region is deleted. Locating this gene explains, in part, why dyslexia occurs and could lead to early and more accurate diagnoses and more effective educational programs for dyslexic children.

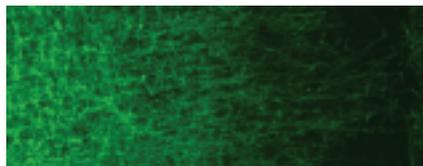
—Pat McCaffrey

New twist on experiment unleashes the brain's potential for healing

When we pour concrete for a sidewalk or foundation, we want the material to be as fluid as possible, so that it will easily assume the shape we have in mind. But for our structure to be durable and useful, we want the concrete to harden—quickly.

The brain's early development is a similarly delicate balancing act between malleability and permanence. The areas of an infant's cerebral cortex devoted to sensory systems are highly plastic, so that cortical circuits can be efficiently sculpted in response to the sights, sounds and smells that make up the baby's world. But as soon as a baby has had enough time to acquire adequate sensory experience—a developmental window known as the “critical period”—neural circuits become hard-wired.

Fixed neural circuits ensure that cortical function is stable and reliable, but stability comes at a cost: if the brain or spinal cord is damaged by trauma,



AARON MCGEE

Stephen Strittmatter and colleagues used a fluorescent green marker to stain myelin in the cortex. Myelin contains the Nogo protein, which prevents the repair of damaged neural circuits. In recent experiments they found that knocking out the Nogo receptor permitted increased plasticity and healing.

disease or stroke, it can rarely repair itself well enough to restore function.

How the brain shuts the door on plasticity and how that process might be blocked to regenerate or repair neural circuits are the focus of the laboratory of Stephen M. Strittmatter, M.D., P.H.D., the Vincent Coates Professor of Neurology.

In 2000, Strittmatter identified a protein called Nogo that suppresses self-repair in damaged axons. In order to establish whether Nogo shuts down plasticity more generally, Strittmatter and Nigel W. Daw, P.H.D., professor of ophthalmology and visual science, married genetic techniques with a classic experiment devised by Nobel prize-winning neurobiologists David H. Hubel, M.D., and Torsten N. Wiesel, M.D., in the early 1960s.

Normally the visual cortex is divided equally between inputs from each eye into regions known as ocular dominance columns, but Hubel and Wiesel showed that if one of an animal's eyes is kept shut during the highly plastic critical period, the active eye's inputs will appropriate a larger share of the visual region, leaving vision in the other eye irreversibly impaired. However, as reported in the September 30 issue of *Science*, when Strittmatter, Daw and postdoctoral fellows Aaron W. McGee, P.H.D., and Yupeng Yang, P.H.D., performed the same experiment with mice specially bred to lack a functional Nogo receptor, the cortex remained plastic after the critical period, and an active eye could usurp cortical real estate from a deprived eye well into adulthood.

Encouraged by these and other results, Strittmatter is searching for Nogo blockers that he hopes will revive the capacity for plasticity, and healing, of the damaged or diseased brain and spinal cord. “Limited nerve cell regeneration and plasticity are central to a range of neurological disorders,” he said, “including stroke, head trauma, multiple sclerosis and neurodegenerative disease.”

—Peter Farley

et cetera ...

PROTECTION AGAINST MAD COW

In 1996, during an epidemic of mad cow disease—bovine spongiform encephalopathy—in British cattle, epidemiologists predicted that up to 100,000 people could contract variant Creutzfeldt-Jakob disease (vCJD), a rapidly progressing, invariably fatal neurodegenerative condition, from infected beef. But that nightmarish scenario has not yet come to pass: 10 years later, only 151 cases of vCJD have been verified.

Laura M. Manuelidis, M.D. '67, HS '70, FW '70, professor and chief of surgery (neuropathology), may have discerned why. Manuelidis and colleagues reported in *Science* in October that exposure to less-virulent strains of CJD may protect against infection with the newly evolved bovine strain. The team found that when neuronal cell cultures were infected with either a weak or sporadic form of CJD, or with agents that cause sheep scrapie, a disease similar to CJD, they resisted infection by the more-virulent strain.

—P.F.

TASTE AND SMELL—THE NOSE KNOWS

Although our taste buds distinguish sweet, sour, salty, savory and bitter, flavor arises from a combination of tastes with odors that enter our nasal passages through the back of the mouth. These “retronasal” odors get special treatment from the brain, according to a new study led by Dana Small, M.Sc., P.H.D., assistant professor of surgery (otolaryngology) and psychology at Yale and an assistant fellow at the John B. Pierce Laboratory.

In a report published in *Neuron* in August, Small and colleagues at Yale and in Germany inserted tubes that pumped odors such as chocolate into subjects' noses, either to the front of the nostrils or to the back of the nasal cavity. They found that a single odor could activate different brain regions, depending on the route it traveled. Odors presented retronasally activated brain areas devoted to the mouth, which Small said is “evidence of the existence of distinct olfactory subsystems”—one specialized for sensing objects at a distance, the other for sensing objects in the mouth.

—P.F.

Coping with life's everyday fears

Drawing lessons from trauma, author offers parents advice on a child's anxieties, large and small.

It was 3 a.m. on a summer night in 2004 when the sound of a pager awoke psychoanalyst Steven R. Marans, M.S.W., Ph.D. The New Haven police were summoning him to a home where three children had witnessed a murder. Along with colleagues in the city's Child Development-Community Policing Program (which Marans founded with the late Donald J. Cohen, M.D. '66, in 1991), Marans invited the children to draw pictures and to talk about any aspects of the event they wished to discuss.

As a nationally known expert on children facing severe trauma, Marans spends much of his time helping children and those who care for them to cope with major upheavals—domestic violence, school shootings, the 9/11 attacks and such natural disasters as Hurricane Katrina. Since 2000 he has also directed the National Center for Children Exposed to Violence, a federal program based on Yale's partnership with the New Haven police.

Now Marans, professor of child psychiatry and psychiatry at the Yale Child Study Center and in the department of psychiatry, has applied his insights to writing a guide for parents that explores the day-to-day challenges of growing up. In his first book for a general audience, *Listening to Fear: Helping Kids Cope, From Nightmares to the Nightly News*, Marans suggests that children's reactions to stress have a common source. Whether the stressor is as extreme as witnessing a murder or as ordinary as coping with teasing, the common source is fear.

Marans, who has been trained in both child and adult psychoanalysis, shows in his book how fear enters into everyday events with a description of a supermarket tantrum by his toddler son (now a college student). For the child, fear played a role—perhaps he feared his lack of competence when his father had to lift him to reach a container of sour cream. Most likely the child also scared himself with his outburst. But the incident stirred Marans' own fears: loss of control, loss of his self-image as someone skilled in understanding children—and loss of face as he imagined onlookers judging him a bad parent. Those fears Marans could explain rationally.

Steven Marans draws on clinical research and his own experiences to explore the fundamental fears all people share.



TERRY DAGRAZI

Marans says that children's fears also evoke their parents' suppressed fears, fears that stem from the normal course of development and from their own childhood experiences.

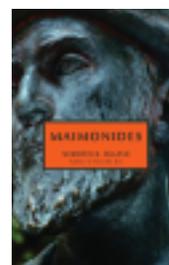
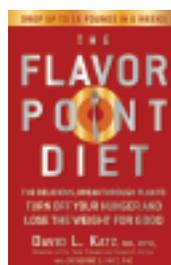
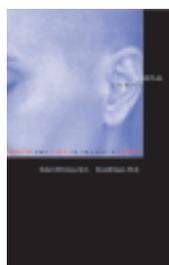
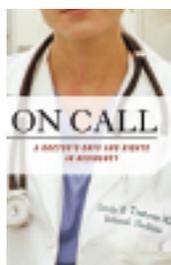
"We desperately want to wave the proverbial magic wand and wave our children's feelings away, not only because we don't like to see our children unhappy but also because it stirs up our own feelings—feelings that we're reminded of by our kids' experiences," said Marans.

Drawing on clinical research and his own experience, Marans said all people share five fundamental fears: loss of life (of loved ones and of oneself); loss of the love of others and for ourselves; bodily harm; losing control of our feelings, impulses or thoughts; and losing the assumed predictability of daily life. By distinguishing our own fears from our child's, Marans said, we become better parents. We need to listen, not only to words but also to behavior, which may be the child's only means of expressing distress.

"My interest in extreme situations is an extension of the concern that I always have: how we use our understanding of human behavior and human development as a way of illuminating people's experience," said Marans during an interview at the Child Study Center. "What I hope the book does is remind us that the worst of our fears, fears that can reach overwhelming or dramatic proportions, are elaborations of the basic fears and anxieties that are part of who we are as human beings. Discovering that there is, in fact, sense to what we feel and how we act can be tremendously reassuring."

—Cathy Shufro

Bookshelf is a column focusing on matters related to books and authors at the School of Medicine. Send ideas to Cathy Shufro at cathy.shufro@yale.edu.



<None>Smoking 101: An Overview for Teens

by Margaret O. Hyde and John F. Setaro, M.D., HS '86, FW '92, associate professor of medicine (cardiology) (Twenty-First Century Books) This book provides information that will help teenagers considering whether to try cigarettes. For teens who already smoke, the authors describe programs and techniques for quitting and list websites of organizations that can help.

On Call: A Doctor's Days and Nights in Residency

by Emily R. Transue, M.D. (St. Martin's Press) While a resident at the University of Washington, Transue, Yale College Class of 1992, wrote about her patients as a way to guard against burnout and share her experiences with friends and family. This collection of stories conveys the atmosphere of overwork, exhaustion and insecurity in which a resident works, as well as Transue's compassion for her patients.

Mortal Secrets: Truth and Lies in the Age of AIDS

by Robert Klitzman, M.D. '85, and Ronald Bayer, PH.D. (The Johns Hopkins University Press) The authors provide a portrait of moral, social and psychological decision making by drawing on interviews and testimonies from more than 70 gay men and women, intravenous drug users, sex workers, bisexual men and heterosexual men and women. For those who are HIV-positive, decisions about disclosure of their diagnosis make them confront intimate questions about truth, lies, sex and trust.

Shields' Textbook of Glaucoma

edited by R. Rand Allingham, M.D., Karim F. Damji, M.D., Sharon F. Freedman, M.D., Sayoko E. Moroi, M.D., PH.D., George Shafranov, M.D., associate professor of ophthalmology and visual science, and M. Bruce Shields, M.D., the Marvin L. Sears Professor of Ophthalmology and Visual Science (Lippincott Williams & Wilkins) Readers will find updated information on the cellular and molecular biology of the eye, molecular genetics of glaucoma and congenital and developmental glaucomas. The book also describes management of glaucoma and approaches to treatment. Each chapter includes summaries of key points.

Psychological Aspects of Reconstructive and Cosmetic Plastic Surgery: Clinical, Empirical and Ethical Perspectives

edited by David B. Sarwer, PH.D., Thomas Pruzinsky, PH.D., Thomas F. Cash, PH.D., Robert M. Goldwyn, M.D., John A. Persing, M.D., professor of surgery (plastic) and neurosurgery, and Linton A. Whitaker, M.D. (Lippincott Williams & Wilkins) This volume examines the relationships among physical appearance, body image and psychosocial functioning. The authors detail the psychological implications of specific disfigurements and of reconstructive procedures, and discuss bioethical, professional and legal issues.

The Flavor Point Diet: The Delicious, Breakthrough Plan to Turn Off Your Hunger and Lose the Weight for Good

by David L. Katz, M.D., M.P.H. '93, associate clinical professor of public health, and Catherine S. Katz, PH.D. (Rodale Books) This book introduces readers to the Flavor Point Diet and provides menu plans and recipes. By combining foods selected by flavor, the regimen "tricks the brain into being satisfied all day."

Globalization, Women, and Health in the 21st Century

by Ilona S. Kickbusch, PH.D., former professor of public health, Kari A. Hartwig, DR.P.H., assistant clinical professor of public health, and Justin M. List, M.DIV. '04 (Palgrave Macmillan) This book explores the complex set of interdependencies among gender, health and globalization.

The Psychotherapist's Own Psychotherapy: Patient and Clinician Perspectives

edited by Jesse D. Geller, PH.D., associate clinical professor of psychiatry, John C. Norcross, PH.D., and David E. Orlinsky, PH.D. (Oxford University Press) The first-person narratives, clinical wisdom and research findings gathered in this book offer guidance for providing effective treatments to patients who are also therapists.

Medical Complications During Pregnancy, 6th ed.

edited by Gerard N. Burrow, M.D. '58, HS '66, the David Paige Smith Professor Emeritus of Medicine and dean emeritus, Thomas P. Duffy, M.D., professor of medicine (hematology), and

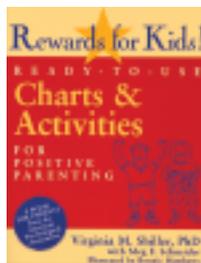
Joshua A. Copel, M.D., FW '85, professor of obstetrics, gynecology and reproductive sciences and of pediatrics (W.B. Saunders) This reference book presents multidisciplinary coverage of the full spectrum of complications associated with pregnancy. Postpartum depression and bioethics are two of the topics covered.

Foundations of Anesthesia: Basic Science and Clinical Practice, 2nd ed.

edited by Hugh C. Hemmings Jr., PH.D. '86, M.D. '87, and Philip M. Hopkins, M.D. (Elsevier) International experts provide complete coverage of basic and clinical science in anesthesiology, emphasizing the principles and clinical applications of molecular and cell biology, physiology, pharmacology and physics and measurement.

Maimonides

by Sherwin B. Nuland, M.D. '55, HS '61 (Schocken Books) Maimonides was a physician, a Torah scholar, a community leader and a philosopher who attempted to reconcile scientific knowledge with faith in God. He was a Jew living in a Muslim world, a rationalist living in a time of superstition. Nuland gives us a portrait of Maimonides that makes his life, his times and his thought accessible to the general reader.



Get Hired! How to Land the Ideal Federal Job and Negotiate a Top Salary

by Lily Whiteman, M.P.H. '90 (FPMI Solutions) This book, based on the experiences of people who found federal jobs, provides tips for breaking into the federal job market—from entry-level to executive positions. The author provides strategies for finding domestic and overseas openings, lists the latest federal jobs websites and offers tips for mastering online applications.

Reconceiving the Gene: Seymour Benzer's Adventures in Phage Genetics

by the late Frederic L. Holmes, Ph.D., the Avalon Professor of the History of Medicine and chair of the Section of the History of Medicine, and edited by William C. Summers, M.D., Ph.D., professor of therapeutic radiology and of molecular biophysics and biochemistry (Yale University Press) More than any other individual, biologist Seymour Benzer is considered to have led geneticists from the classical gene into the molecular age. Drawing on Benzer's record of his experiments, correspondence and published sources, this book reconstructs how the former physicist initiated his work in phage biology and achieved his landmark investigation.

Nuclear Cardiology, the Basics: How to Set Up and Maintain a Laboratory

by Frans J.Th. Wackers, M.D., Ph.D., professor of diagnostic radiology and medicine, Wendy Bruni, and Barry L. Zaret, M.D., the Robert W. Berliner Professor of Medicine and professor of diagnostic radiology (Humana Press) This guide offers a concise, action-oriented plan for solving the many practical and technical problems involved in establishing and running a nuclear cardiology lab. The authors answer basic questions about purchasing equipment and determining space requirements.

Rewards for Kids! Ready-to-Use Charts & Activities for Positive Parenting

by Virginia M. Shiller, Ph.D., lecturer in the Child Study Center, and Meg F. Schneider (Magination Press) This book shows how to motivate children to improve their behavior and fulfill their responsibilities, using a variety of child-friendly sticker charts and other tools. The authors teach parents positive techniques for helping children to overcome such common behavior problems as bedtime procrastination and fighting with siblings.

The descriptions above are based on information from the publishers.

SEND NOTICES OF NEW BOOKS TO Cheryl Violante, *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612, or via e-mail to cheryl.violante@yale.edu

Consortium seeks to boost minority presence in health information professions

A senior at Hill Regional Career Magnet High School in New Haven, Jordon Thomas was impressed when he first set foot in the Cushing/Whitney Medical Library last summer. "I didn't know there were so many resources that were right in front of me," said Thomas, who attended a science program sponsored by the School of Medicine.

Thomas is just the type of student that Charles J. Greenberg, M.L.S., M.Ed., coordinator of medical library curriculum and research support, would like to attract to the health sciences information professions: a college-bound minority student who might consider becoming a medical librarian or health information specialist. (As it turns out, Thomas, who is African-American, plans to be a pharmacist.) Greenberg is the project coordinator for a newly formed consortium of eight university medical libraries that is trying to interest minority students in careers in medical librarianship. Nancy K. Roderer, M.L.S., former director (1992-1999) of Yale's medical library and now director of the William H. Welch Medical Library at Johns Hopkins, is the principal investigator. Funded with a three-year, \$640,000 matching grant from the federal Institute of Museum and Library Services, the group comprises Yale, Georgetown University, Houston Academy of Medicine, Howard University, the University of Colorado at Denver, Johns Hopkins University, the University of Tennessee and Washington University in St. Louis. Currently, 9 percent of medical librarians are members of minority groups.

The effort to interest minority students is part of a broader attempt to recruit health care professionals who reflect the ethnic and racial diversity of their patients. "Health care providers are very concerned with cultural competence," said Greenberg. "We want to become part of that mosaic of health careers." The medical librarianship project is just in the planning stage, but libraries in the group plan to sponsor tours, internships and other outreach programs.

The group's task in part is to replace the image of a dowdy librarian with a more up-to-date view of a computer-savvy "information specialist."

Yale's medical library has been "at the forefront of the university's partnerships with the New Haven public schools," said Claudia R. Merson, director of public school partnerships at the Office of New Haven and State Affairs. For instance, Yale medical librarians taught Internet skills to Career High School teachers and administrators in the mid-1990s. "This is another opportunity," said Merson. "There's been so much exposure to health professions, but librarianship has not been one of them. It's new and exciting, and it looks like it's going to be cool."

The project's website is <http://www.bioinfo-career.org/>.

—Cathy Shufro

In Circulation is a column focusing on activities at the Cushing/Whitney Medical Library. Send ideas to Cathy Shufro at cathy.shufro@yale.edu.



PAUL CARLTON

Emergency care in the wake of Katrina

If there was a good news story about Hurricane Katrina, it was the medical response to the disaster, said Paul K. Carlton Jr., M.D., director of the Office of Homeland Security of the Texas A&M University System Health Science Center. Speaking at the Yale New Haven International Congress on Disaster Medicine and Emergency Management in September, Carlton described how emergency “surge” hospitals mobilized to handle thousands of patients in Baton Rouge.

“Your worst nightmare is to lose an entire medical network, and that is what happened in Katrina,” said Carlton, a proponent of the surge concept, in which hospitals expand facilities or open new ones in emergencies. Within days, he said, health and disaster teams had set up four surge hospitals in Baton Rouge, including one at a former Kmart store that had been closed for 10 years. “It was filthy,” Carlton said. Crews found portable air-conditioning units, got power to the building, bought portable toilets and converted the big-box store into a 1,000-bed hospital.

Driving the medical teams, Carlton said, was a basic principle: “We will not break trust with our patients.”

—John Curtis



JUDAH FOLKMAN

Bright future for a roller-coaster compound?

In 1998, Endostatin, a protein that inhibits blood vessel growth, was touted as a silver bullet for cancer after tests in mice showed it killed tumors by cutting off their blood supply. But six years later, the future looked bleak: *Fortune* magazine said the angiogenesis inhibitor “failed dramatically” in clinical trials, and EntreMed, a Maryland biotech company, abandoned the drug in 2004 after flirting with bankruptcy.

But Endostatin is not dead yet, according to its creator, Judah Folkman, M.D., who spoke at Yale in October. Folkman, a Harvard researcher, said both reports exaggerated the reality. His work led to FDA approval in 2004 of another angiogenesis drug, Avastin, which is expected to reach \$6 billion in sales and may become the largest-selling anticancer drug in history.

Three weeks before Folkman’s Yale talk, China approved an Endostatin product developed and tested by the Chinese biotech company Medgenn. A trial involving 493 late-stage lung cancer patients showed that its Endostar drug was effective, doubling survival time from three to six months when combined with chemotherapy. Folkman hopes the Chinese findings will revive the future of Endostatin in the American market. “It’s had a tough life,” he said, “but it’s been resuscitated.”

—Michael Fitzsosa



JACK EL-HAI

A pioneering lobotomist’s mixed legacy

When he began his biography of Walter J. Freeman, M.D., a Yale College graduate who pioneered lobotomy in the United States, journalist Jack El-Hai expected he would be writing about “a monster.”

The truth was more complicated, said El-Hai, author of *The Lobotomist: A Maverick Medical Genius and His Tragic Quest to Rid the World of Mental Illness*, speaking at a master’s tea at Yale in November. Psychiatrists embraced the crude surgery that severed neural pathways between the frontal lobes and the thalamus, El-Hai argued, because until the advent of Thorazine in 1954 they had few effective treatments for psychiatric illnesses. “They were willing to try something experimental, something desperate. ... because at least it held out some hope,” said El-Hai.

From 1936 to 1967 roughly 40,000 patients underwent lobotomies nationwide, for conditions ranging from depression to schizophrenia. Freeman did 3,400 of them, including one on a sister of John F. Kennedy. Some patients felt better, some became disabled and 2 percent died.

Freeman, El-Hai noted, “was one of the few advocates of a biological orientation for psychiatry. That is his most positive legacy today, if you can find one.”

—C.S.



DIKEMBE MUTOMBO

NBA star makes a giant impact in his African homeland

As he walked through campus last September, Dikembe Mutombo, all-star center for the Houston Rockets, cut a somewhat startling figure. With an impeccably tailored deep-blue suit draped over his 7-foot, 2-inch frame, Mutombo towered over his hosts like a grade-school teacher minding charges on a field trip.

He came to Yale at the invitation of Anup Patel, a second-year medical student who had heard of the Dikembe Mutombo Foundation’s humanitarian work in Mutombo’s native Democratic Republic of Congo (DRC). Mutombo contributed \$10 million for the construction of a 300-bed hospital in the capital of Kinshasa, which will open in June to provide care to the city’s poorest residents and to train its health professionals. Yale and the foundation are considering a partnership that would provide opportunities for medical students to travel to the DRC for clinical clerkships.

“I grew up poor and I never forgot where I came from,” said Mutombo, in an address at Battell Chapel. “If I was going to do something that will carry my legacy, I wanted to make sure it was very good, that it will stop the suffering, that it will help the people that don’t have a chance to go on a plane to go to South Africa or Europe to get treatment.”

—Peter Farley



Harvey Cushing

the man, the surgeon and the father

By Peter Farley

A new biography of the pioneering neurosurgeon explores different facets of the man who revolutionized brain surgery.



CUSHING/WHITNEY MEDICAL LIBRARY (2)

J. Michael Bliss, PH.D., author of a new biography of Harvey W. Cushing, M.D., assumed the lectern at the Hope Auditorium last October to face what a Catskills comic might call a tough crowd: Cushing's descendants and relatives, who had gathered to celebrate the renowned neurosurgeon's life and to plan for a permanent home at Yale for Cushing's rich collection of brain specimens, photographs, drawings and memorabilia.

But Bliss, a historian at the University of Toronto, proceeded without fear or favor as he discussed his book, *Harvey Cushing: A Life in Surgery*, and wasted no words in raising an issue of interest to those with a personal connection to the notoriously demanding Cushing. "There's vigorous debate about Cushing's professional motives and his professional personality, and this is the kind of thing we have to talk about so long after his death," Bliss declared. "The question is whether or not he was an egotistical, hard-driving, selfish, mean son-of-a-bitch."

Perhaps to smooth the way for that question, Bliss first emphasized that Cushing, an 1891 Yale College graduate and one of the most lauded figures in the history of medicine, truly was as great as his admirers would have it. In diligence, innovation and pure skill, Bliss said, Cushing—father of modern neurosurgery, artist, Pulitzer Prize-winning biographer of Sir William Osler and more—had no equal. Before Cushing, patients routinely bled to death during intracranial surgery, which had a mortality rate approaching 50 percent. Thanks to his introduction of rigid haemostasis, asepsis, electrocoagulation and other procedures, mortality rates plummeted to 10 percent.

In his professional life Cushing was a "tough hombre" who "reduced nurses to tears and residents to nervous breakdowns with withering scorn and sarcasm," Bliss said. Cushing's punishing schedule—including regular 98-hour weeks—exacted a toll on his wife and children, who "found it difficult to relate

to their stern Victorian father, who disapproved of jazz, the movies, fashionable dress, telephone calls, boyfriends, women in medicine, women smoking—probably women at college—and young men who did not attend to their studies and the need to get on with qualifying for Yale."

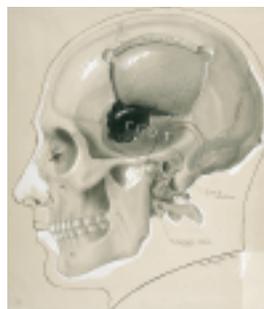
His patients, however, knew another Cushing. "His bedside manner was absolutely wonderful; his dedication to his patients absolutely boundless," Bliss said.

Cushing's reaction to his son Bill's death poignantly captured his complex sense of duty. While Cushing was teaching surgery at Harvard Medical School and the Peter Bent Brigham Hospital in Boston, Bill died in an automobile accident after a night celebrating the end of his junior year at Yale. Cushing "called [his wife] Kate to tell her, then carried out a scheduled operation, which was a success, then told his team about the family tragedy and left for Connecticut to claim his son's body."

Though Cushing spent almost his entire professional life at Johns Hopkins and at Harvard, his undergraduate years at Yale College were so formative and important to him that he returned to Yale at the end of his surgical career to be Sterling Professor of Neurology and director of studies in the History of Medicine. There could be no more appropriate place than the School of Medicine to house the Cushing Collection, Bliss said.

"He was one of Yale's most illustrious graduates, and the preservation of his work and legacy at Yale—his books, his papers, and now his wonderful collection of patient photographs and specimens—is a fitting aspect of the university's service to generations past, present and future. Although Harvey Cushing learned a lot and did a lot at Johns Hopkins and at Peter Bent Brigham," Bliss said, "Yale was his alpha and his omega."

Peter Farley is a contributing editor of *Yale Medicine* and the managing editor of the medical school's bimonthly newsletter, *Medicine@Yale*.



CUSHING BRAIN TUMOR REGISTRY (2)

OPPOSITE TOP Harvey Cushing in 1907 at his desk at Johns Hopkins, six years after he began his residency under the tutelage of surgeon William Stewart Halsted. While at Hopkins, Cushing rose to fame as a neurosurgeon and an expert in the pituitary gland.

OPPOSITE BOTTOM An undated photo of a Cushing operating room. Cushing's innovations in intracranial surgery reduced mortality rates from about 50 percent to 10 percent.

ABOVE Throughout his career Cushing kept meticulous records of his cases, including photographs of his patients, such as this one showing a surgical incision. He also made detailed drawings of the brain. His collection of notes, microscopic slides, brain specimens and photographs are now known as the Cushing Brain Tumor Registry. The knowledge gleaned from the registry revolutionized the practice of neurosurgery.

Yale connections around the world

A medical student's summer research journey becomes a Yale—and family—reunion like no other.

By Jill Max



TERRY DAGRADI

Medical student Tamara Lazic traveled to Italy last summer for a research project with her advisor, interventional radiologist Robert White. During her stay she was reunited with her mother, who lives in Serbia, and introduced to a world of Yale connections.

When Tamara Lazic, now a second-year student at the School of Medicine, sought to combine a passion for languages with research for her thesis, she had no idea the project would take her halfway around the world to work in a clinic where a Yale physician collaborating with a former Yale fellow would perform a life-changing procedure on her mother.

A native of Belgrade, Serbia, Lazic traveled to Los Angeles in 1999 to live with her father, and in 2004 came to New Haven, after graduating from UCLA with a degree in physiological science. Like many students at the School of Medicine, she wanted to begin research for her thesis during the summer between her first and second years. But Lazic, who speaks Serbo-Croatian, English, Spanish and some Russian, also wanted to learn another language. She set her sights on Italy, which had the added bonus of being located just across the Adriatic Sea from her mother, a legal advisor in the Ministry of Internal Economic Relations of Serbia and Montenegro.

While researching overseas projects, Lazic came across the work of Robert I. White Jr., M.D., professor of diagnostic radiology and director of the Yale Vascular Malformation Center. An interventional radiologist, White travels widely to treat patients and educate physicians about hereditary hemorrhagic telangiectasia (HHT), a vascular disorder. Patients with HHT, also called Osler-Weber-Rendu syndrome, lack the capillaries that normally form between arteries and veins. This lack creates fragile sites that can rupture and bleed due to the flow of high-pressure arterial blood directly into veins. About 95 percent of people with HHT have recurrent nosebleeds, but lesions and malformations can occur in many parts of the body. Defects in smaller blood vessels, such as those inside the nose or on the skin, are known as telangiectases, while those in the larger blood vessels in the liver, lungs, brain and gastrointestinal tract are called arteriovenous malformations (AVMs). HHT affects approximately one person in 5,000, involves multiple organs and often goes undiagnosed. White has been on a mission to understand and treat HHT since 1990, when he

helped found the Hereditary Hemorrhagic Telangiectasia Foundation International (www.hht.org). Since then he has been instrumental in establishing 20 HHT Centers of Excellence in the United States, Europe and Japan. “For every 100 patients with HHT, 40 have lung or brain malformations, and half of those will be disabled or die prematurely from something that can be fixed,” he said. Treatment usually involves embolization, a minimally invasive procedure in which the blood supply to the abnormal blood vessels is cut off.

White’s enthusiasm for the HHT cause is contagious, and Lazic quickly signed on to spend last summer at the HHT center at the University of Bari in southern Italy, where she did research on diffuse pulmonary AVMs, the most severe form of the disease, in which multiple AVMs form in one or both lungs. White has close ties to the Bari center, which he visits twice a year to help treat patients. The center was established thanks to HHT patient Nicola Signorile, whom White met at a conference in Denmark in 1999. Signorile, a retired accountant, had suffered severe nosebleeds for 30 years before being diagnosed with HHT in 1997, but had been unable to find a physician to treat him. White encouraged him to seek out a physician in Italy who would be interested in learning more about diagnosing and treating the disease. Signorile’s search led him to Carlo Sabbà, M.D., FW ’90, a professor of medicine at the University of Bari, who had completed a two-year hepatology fellowship at Yale in 1990. Signorile introduced Sabbà to White at a conference in Toronto in 2000 and Sabbà was hooked: with the help of university President Giovanni Girone, a college classmate of Signorile, the University of Bari opened the Interdepartmental HHT Center in 2001 with Sabbà as its director.

Four years after it opened, the Bari center now treats 300 families from all over Italy and southern Europe. “Our center came about as Yale’s offspring, but is now growing into a beautiful adolescent,” said Sabbà. White has helped train doctors there to repair AVMs and continues to assist in complex cases during his regular visits. In 2005 he convinced Signorile, who had suffered a cardiac arrest following a severe nosebleed in which he lost two liters of blood, to come to Yale for a septal dermoplasty, a procedure perfected by Yale HHT team member Douglas A. Ross, M.D., associate professor of surgery (otolaryngology). Last June Signorile underwent the procedure, which involves replacing the lining of the nose with a skin graft from the thigh. He couldn’t be happier with the results. “It was

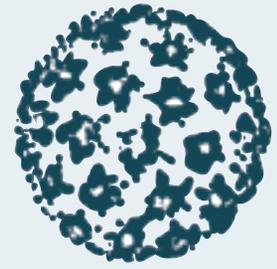
extraordinary,” he said. “I want everyone to know, because people are afraid of this operation, especially in Italy.”

Meanwhile, Tamara Lazic’s mother, Vesna Lazic, 51, had a different problem. She had been suffering from pelvic pain and bleeding so severe that it was sapping her energy and making her daily activities difficult. When Lazic showed White her mother’s medical records, he suspected, correctly, uterine fibroids. In his travels, White also teaches uterine-fibroid embolization, a procedure similar to the one used to treat AVMs, in which the fibroid’s blood supply is cut off, literally starving the tumor to death. Viewing Vesna Lazic’s case as both a teaching opportunity (the procedure is unavailable in Serbia and had not been done at Bari) and a chance to help both her and her daughter, he offered to perform the procedure in Bari. Sabbà and Girone immediately arranged to accept Vesna Lazic as a patient at no charge, but the next obstacle was getting her to Italy. It normally takes a month to obtain a visa to enter Italy from Serbia, but White had to leave the country in just a few days. Girone used his contacts at the Italian embassy in Belgrade to prevail upon authorities to speed the process.

Lazic and her mother see each other only once a year, and were overjoyed to be reunited and to resolve Vesna Lazic’s medical problems. Vesna Lazic arrived in Bari in August; White successfully performed the embolization and taught doctors there how to do the procedure. “It opened a lot of doors for them,” said Lazic, who is grateful for the help she and her mother received.

Looking back, Lazic is amazed at the turn of events that led to her mother’s uterine-fibroid embolization. As a Yale medical student, she traveled 3,000 miles for her thesis project, where she met a former Yale patient, worked with a Yale-trained specialist in a center whose existence was sparked by Yale research and saw “image-guided therapy” performed on her mother by a Yale physician. All these encounters were in a sense made possible by Sanford G. Bluestein, M.D. ’46, a retired radiologist who is sponsoring Lazic’s medical education through a scholarship fund he established in 1996. It’s quite a journey for a young woman who grew up in war-torn Serbia and who sees the opportunity to attend Yale as a dream come true. “If you told me six years ago that I would end up at Yale,” she said, “I wouldn’t have believed you.”

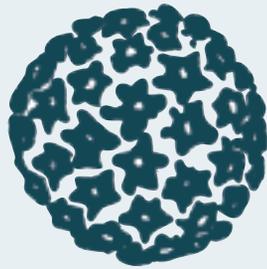
Jill Max is a freelance writer in Connecticut.



One in 10 human cancers starts with a viral infection, often the ubiquitous human papillomavirus. Yale scientists want to know why—and are hot on the trail of new vaccines and therapies to treat

the virus

behind the cancer



By Jennifer Kaylin

Illustrations by Yasuo Tanaka

Photographs by Terry Dagradi

More than 50 years ago, a young woman named Henrietta Lacks was diagnosed with cervical cancer. Despite surgery and aggressive radiation therapy, the cancer soon spread throughout her body, and on October 4, 1951, she died.

It was a cruel death for the 31-year-old mother of five, but Lacks' story didn't end there. George O. Gey, M.D., head of tissue culture at Johns Hopkins University, where Lacks was treated, had been searching, for research purposes, for a line of human cells that could live indefinitely outside the body. He got his wish when cells from Lacks' cancerous tumor were cultured. Just as they had done in her body, the cells multiplied ferociously in the lab, crawling up the sides of test tubes and consuming the medium around them. An entire generation of the cells reproduced every 24 hours.

Referring to Lacks' cells, Gey declared at the time, "It is possible that, from a fundamental study such as this, we will be able to learn a way by which cancer can be completely wiped out." To this day, Lacks' cells, known as the HeLa cell line, are some of the most robust and rapidly growing cells known to science. They are still used by thousands of researchers around the world to decipher the complexities of cell biology, particularly as they apply to cancer.

At Yale, scientists are using the HeLa cell line to study, among other things, the human papillomavirus (HPV) that

causes the cervical cancer that killed Lacks. "Her legacy," says Daniel C. DiMaio, M.D., PH.D., the Waldemar Von Zedtwitz Professor of Genetics and professor of therapeutic radiology, "is that her cells are helping us unravel the pathogenesis of cervical cancer, so that some day we might be able to prevent and treat it. It's rather remarkable."

The field of human tumor virology is still a relatively new area of scientific inquiry. Although it has been known for nearly a century that viruses can cause tumors in animals, only in recent decades have human tumor viruses been identified. Researchers at Yale, among them I. George Miller, M.D., have contributed to our understanding of the mechanisms of viral tumorigenesis.

Miller, the John F. Enders Professor of Pediatrics and professor of epidemiology and of molecular biophysics and biochemistry, was the first to show that a human virus can cause tumors in primates. Experiments he conducted at Yale in the 1960s showed that the Epstein-Barr virus (EBV) could cause lymphoma in cotton-top marmosets. He also showed that the virus was very effective at changing normal human lymphocytes into cells with properties of cancer cells in culture.

More recently, DiMaio's lab demonstrated that cervical cancer cells need the viral proteins to grow, thus raising the possibility that the cancers can be treated with antiviral



drugs. DiMaio, Janet L. Brandsma, Ph.D. '81, and others are currently working on a vaccine to treat patients with cervical cancer.

Besides these advances, Yale researchers who specialize in tumor virology believe their work could have wider applications, potentially expanding knowledge of a range of cancers and other illnesses and biological processes, such as cellular aging. "It will help us understand all cancers," says Brandsma, an associate professor of comparative medicine and pathology. "Most small mutations in cellular genes are very subtle, but with viral cancers, the viral genome in the cancer cell is foreign and easier to recognize. It's an excellent model."

Chickens, rabbits, warts and mice

More than 10 percent of all cancers in humans are strongly associated with infection by tumor viruses, and roughly 15 percent of all cancer deaths worldwide are caused by viruses. "It's a very important problem," DiMaio says. But he also sees tumor virology as a tremendous opportunity. "Once you know that a cancer is caused by a virus, you are far ahead of where you'd be for any other cancer, because you've identified the target, you've identified the cause and you have well-established ways to prevent or treat the disease that just don't exist for spontaneously arising tumors."

To say that certain viruses *cause* certain cancers can be misleading. You can't catch cancer from another person, and most people who are infected with HPV, for example, won't get cervical cancer. However, everyone who gets cervical cancer has the HPV infection. "Other things have to go wrong in order for the cancer to develop," DiMaio explains, "but the virus contributes in an essential way. If you prevent virus infection by vaccination, you don't get the cancer, and if you turn off the virus, the cancer can't grow."

HPV is the best-understood example of how a virus leads to cancer. Two things have to happen: First, viral gene products cause the cells to become genetically unstable and accumulate mutations that render cells unresponsive to

aspects of growth control and the immune response. Second, the viral oncogenes provide a sustained stimulus to cell growth.

The first clue that there was a viral link to certain cancers came in 1911. Using a virus found in chickens, F. Peyton Rous, M.D., a scientist at the Rockefeller Institute for Medical Research, showed that the chicken sarcoma could be induced in other chickens. "There was a lot of doubt about what applicability it had, if any, to human disease," says Miller. But in 1966 Rous shared the Nobel Prize in physiology or medicine for his research on the link between viruses and cancer, and the chicken virus became known as the Rous sarcoma virus.

Another important development, Miller says, came in the 1930s, when Richard Shope, M.D., one of Rous' collaborators and the father of the late Yale epidemiologist Robert E. Shope, M.D., HS '58, was out hunting with a friend. The friend mentioned that he'd seen rabbits with horns—actually giant warts. Shope asked his friend to send him some of the horns, which he then ground up, so he could isolate the virus causing the warts. When he injected the virus into other rabbits, they also grew horns. Interestingly, when New Zealand white rabbits were inoculated with the virus, they grew horns, but Shope couldn't recover the virus; in cottontail rabbits, the virus was retrievable. This discovery raised the question of viral latency, which scientists now know is intrinsic to the behavior and biology of tumor viruses. (Miller is currently researching latency as it relates to the Kaposi sarcoma virus. He's trying to determine what the suppressor mechanism is and why latent-state viral genomes are suppressed in the tumor cells and then periodically reactivated.)

In the early 1950s Ludwik Gross, M.D., head of cancer research at the Bronx (N.Y.) VA Hospital, opened the field of tumor virology in mammals with his discovery of what became known as the Gross mouse leukemia virus. Gross showed that a virus led to mouse leukemia and could be passed from one generation to the next.

Although these and other studies unequivocally showed that viruses can lead to tumors in animals, making



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—Daniel DiMaio

the leap to human tumor viruses wasn't easy. Researchers encountered several obstacles. For starters, only a small percentage of people who are infected actually develop cancer; it takes more than a virus infection for a tumor to form; and other factors, such as immunosuppression or exposure to another carcinogen, must be present. Finally, it can take decades for symptoms to appear.

Despite these challenges, in 1965 the first bona fide example of a human tumor virus—EBV—was discovered in cells from Burkitt lymphoma. Since then scientists have identified six viruses that have been shown to play a role in human cancers.

HPVs are a family of small DNA viruses that typically cause benign warts. However, certain high-risk HPV types have been linked to a variety of carcinomas, the most prevalent being cervical cancer. HPV is also thought to play a role in other anogenital cancers, skin cancers and some head and neck tumors.

Hepatitis B virus and hepatitis C virus are genetically unrelated, but both can cause acute and chronic liver disease, which, under certain conditions, can progress to primary hepatocellular carcinoma. EBV is a herpes virus that can cause mononucleosis. However, EBV has also been linked to Burkitt lymphoma and nasopharyngeal carcinoma, and it has been implicated in some forms of Hodgkin disease and gastric carcinoma. Human herpes virus 8 (HHV-8), also known as Kaposi sarcoma herpes virus, is related to EBV. It was first identified in the tumor DNA of a patient with Kaposi sarcoma, a rare tumor until the AIDS epidemic, when it became one of the most common causes of cancer deaths among AIDS patients. HHV-8 is also believed to play a role in Castleman disease and body cavity lymphoma. Finally, human T lymphotropic virus type 1 leads to a rare tumor, adult T-cell leukemia/lymphoma, in the Far East and the Caribbean basin, as well as to some nonneoplastic diseases.

“It used to be a job to convince people that viruses were an important part of the cancer story. There had been a lot of research, but people just didn't believe it. They won-

dered, for example, why so many people who are infected don't get cancer,” says Miller. “We had to fill in the details. Now people pretty much accept the idea.”

“When I arrived at Yale in 1983, people didn't think these viruses were important to cancer,” DiMaio says. “At conferences the human papillomavirus was always the last talk of the meeting. Now it's taken center stage.” That's partly because, of all the viruses found to play an etiologic role in human cancers, the HPV types (16 and 18) linked to cervical cancer are probably the best-understood and the ones that hold the greatest promise for vaccines to be used for prevention and treatment.

Tight corsets and HPV

Early thinking on cervical cancer and what causes it would hardly suggest such a rosy scenario. In 1842 an Italian physician in Florence observed that married women in the city were getting cervical cancer, but nuns in nearby convents weren't. Although this observation would seem to point to a link between sexual activity and cervical cancer, the physician did not make this connection. He also observed that nuns had higher rates of breast cancer, and suggested that the nuns' corsets were too tight. “Clearly they had no clue,” DiMaio says, “but the observation was significant.”

Beginning in 1975, the virologist Harald zur Hausen, M.D., D.Sc., figured out what had eluded the Florentine physician. Zur Hausen, who for 20 years headed the German Cancer Research Center in Heidelberg, showed that HPV, a common infection spread through skin-to-skin contact and sex, could lead to cervical cancer. He and his research team successfully isolated several genotypes of the virus, some of which they linked to genital warts and others to cervical cancer.

Today, cervical cancer is responsible for 250,000 deaths each year worldwide, according to Charles J. Lockwood, M.D., the Anita O'Keefe Young Professor of Women's Health and chair of the Department of Obstetrics, Gynecology and Reproductive Sciences. In the United States, where early



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Janet Brandsma

screening has greatly reduced the mortality rate due to cervical cancer, about 5,000 women a year still die of the disease.

“From a mortality standpoint, the problem in this country is largely contained, but worldwide it’s a huge problem,” says Lockwood. “From a financial standpoint it remains a major problem in this country. The cost of surveillance and preventive treatments is astronomical (\$200 million a year just for screening), and a woman who has multiple surgical treatments for precancerous conditions of the cervix, such as cone biopsies or loop electrocautery excision procedures, is at a higher risk of giving birth to a preterm baby.”

Even though cervical cancer in this country is largely under control, women still get it, and when they do, it can be devastating. Thomas J. Rutherford, PH.D., M.D., FW ’94, associate professor of obstetrics, gynecology and reproductive sciences and director of gynecological oncology, recalls a patient in her mid-30s who was pregnant. The results of a routine Pap smear were abnormal. A colposcopy revealed a very high-grade squamous cell lesion. To save his patient’s life, Rutherford recommended an immediate radical hysterectomy, but that would have meant losing the baby. “The patient finally agreed,” Rutherford says, “but after the surgery she said to me, ‘I can’t believe I gave up one of my children.’ It was a difficult choice she made, but she probably would have died if she hadn’t.”

Another patient was a 20-year-old college student who had adenocarcinoma of the cervix, which is also caused by HPV. She underwent a cone biopsy, but the Pap smear still revealed abnormalities in her cervical cells, “We couldn’t repeat the procedure, because she wanted to have children,” Rutherford recalls. “We put everything on the table: This is the situation. Your best option is to have a child now.” The patient took Rutherford’s advice and had a baby, after which Rutherford performed a radical hysterectomy. “There she was, getting married, having a baby and then having a hysterectomy, all before she turned 21,” he says. “I assure you that wasn’t what she foresaw for herself.”

Even when a patient isn’t diagnosed with a precancerous lesion, the ordeal of getting a positive test result, going back for more tests and possibly having to have a colposcopy or a biopsy before finally getting a clean bill of health is stressful. “It’s also a very expensive way to prevent cervical cancer,” Brandsma says. “It’s a lot of money and anxiety.”

A far better approach, she and other HPV experts say, would be to vaccinate people against the disease. Researchers at Yale and elsewhere have been working on two types of vaccines with promising results. A prophylactic vaccine being developed at the National Cancer Institute and the University of Washington, among other places, would prevent infection by generating a neutralizing antibody. Brandsma, DiMaio and other researchers at Yale and elsewhere are working on a therapeutic vaccine that would generate killer T-cells that could recognize tumor cells as being foreign and destroy them. “Cervical cancer is the ideal cancer in which to demonstrate the principle of anti-cancer vaccines, because we know what the tumor antigens are. Viral E6 and E7 are the oncoproteins expressed in all lesions. They’re always required,” Brandsma says.

Two versions of the prophylactic vaccine have shown encouraging results in clinical trials. Both prevented persistent infection by the HPV types contained in the vaccine in 100 percent of vaccinated women and reduced cervical abnormalities by more than 90 percent. Merck & Co., the maker of one vaccine, reported in the fall of 2005 that, in a Phase III trial of more than 12,000 women, the vaccine prevented virtually 100 percent of growths that can lead to cervical cancer. The company has since announced plans to file for approval with the U.S. Food and Drug Administration before the end of the year. GlaxoSmithKline, maker of the other vaccine, reported similarly positive results with its clinical trials and plans to seek approval in Europe and other countries in 2006.

Once a vaccine is in widespread use, experts predict an immediate 44 to 70 percent reduction in abnormal Pap smears and a long-term reduction of close to 95 percent



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—George Miller

in cervical cancer rates. As promising as these numbers are, the vaccine also has limitations, chief among them being that three injections are required and the vaccine must be kept refrigerated. Especially in developing countries, where the need for a vaccine is the greatest, these obstacles have the potential to limit the vaccine's efficacy. Another limitation is that, although the vaccine prevents infection by the most common high-risk HPV types, less common high-risk HPV types are not included.

Beyond that, the vaccine raises thorny social issues. To maximize its effectiveness, it should be given to girls between the ages of 9 and 12, before they become sexually active.

Already, some religious groups have raised concerns that this will be interpreted as a license to engage in premarital sex.

"These vaccines could provide a huge public health benefit," Lockwood says. "To allow their introduction to be blocked because of some extreme ideological position is unconscionable and irrational. It would be a huge cost savings, and could save some young person from dying in her 20s or 30s."

Putting cancer genes to sleep

Vaccines are not the only approach to controlling cancers with viral origins. Using the HeLa cell line, which contains HPV DNA, researchers have figured out that the proliferation of cervical cancer cells requires the expression of the HPV oncogenes E6 and E7, which are expressed by cervical carcinoma cells. These oncogenes inactivate the cancerous cells' major tumor suppressor pathways, thereby allowing the cells to proliferate.

An effective way to combat this, scientists have learned, is to induce a biological phenomenon known as senescence, an irreversible suspended animation of the cell, which acts as an important tumor suppressor mechanism. DiMaio and his colleagues have determined that the introduction of the papillomavirus protein E2 to the cell represses E6 and E7, halts cell growth and induces senescence. So, although the tumor cells have accumulated essential mutations, they still

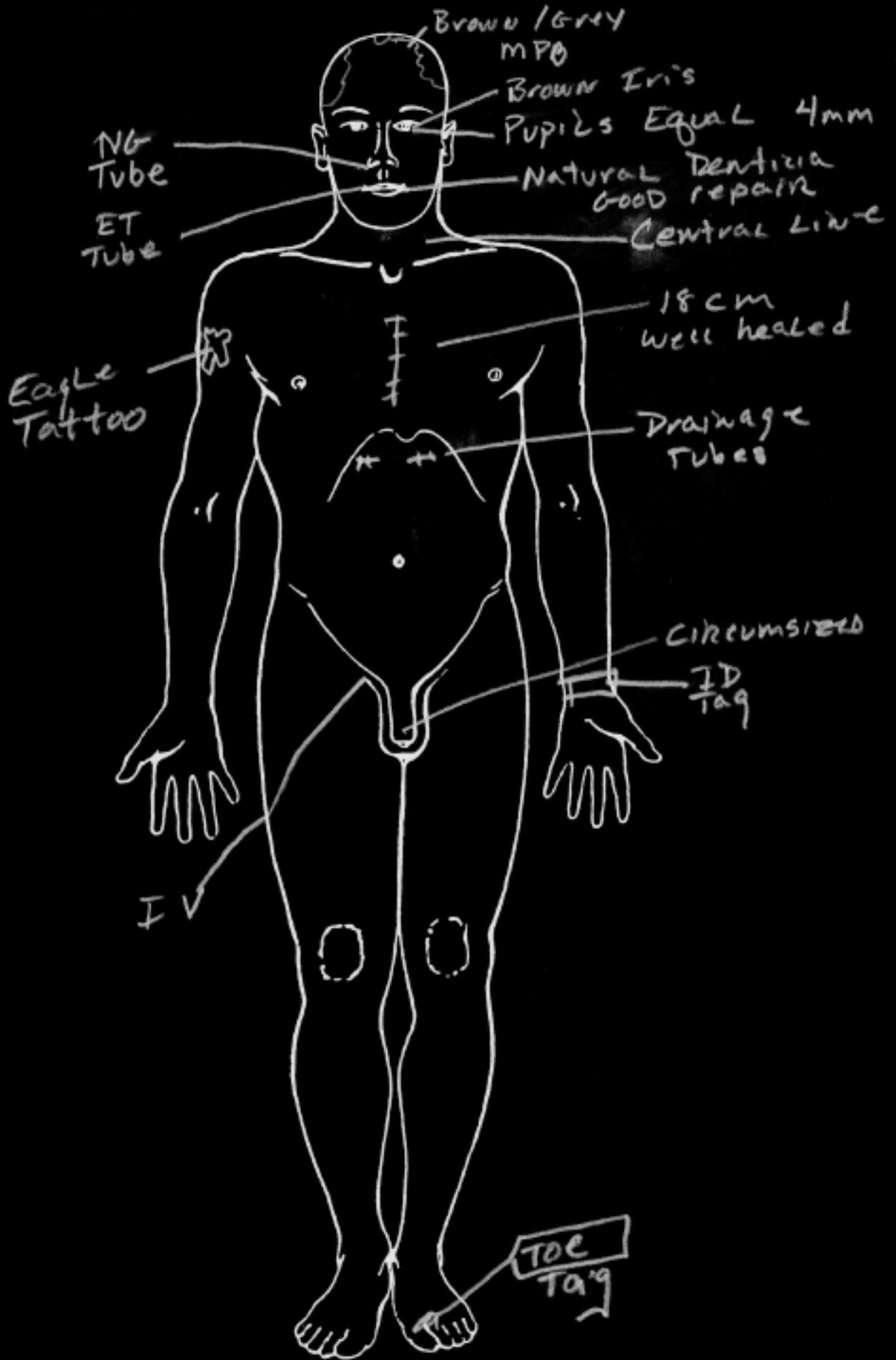
depend on the viral proteins. DiMaio likens it to a house of cards. "You need many cards to build a multistory house, but the whole edifice tumbles down if you remove the crucial card at the bottom.

"When we added E2, it induced senescence in a day or two," DiMaio says. "This creates an important barrier to tumor formation and growth. It also gives us a new model to study senescence." DiMaio says this is important because the hope is that senescence can be applied to other cancers as well. Also, there's great interest in someday inducing senescence to block aging and age-related disease. "Half of my lab is focusing on senescence," he says.

As the study of tumor virology continues to grow in importance and application, a growing number of Yale researchers are investigating other pieces of the puzzle. John K. Rose, PH.D., professor of pathology, is interested in vaccines constructed from virus vectors. He is collaborating with Brandsma's and DiMaio's labs to develop HPV vaccines using a slightly different approach. The same antigen is involved, but instead of injecting DNA into the animal, as Brandsma does, he uses virus vectors. Rose is also in charge of a small unit that has recently recruited two junior tumor virologists. Michael D. Robek, PH.D., assistant professor of pathology, studies replication of hepatitis B virus, and Robert E. Means, PH.D., assistant professor of pathology, studies ways that herpes viruses avoid the immune response.

More than 50 years ago, Henrietta Lacks was helpless against the cancer that destroyed her body, but today, thanks in part to her cells, researchers are closer than ever to defeating that enemy, and the hope is that with the knowledge gained by studying HPV, other cancer-fighting breakthroughs will soon follow.

Jennifer Kaylin is a contributing editor of Yale Medicine.



The final chapter

Once routine, autopsies are rarely performed, and pathologists lament the loss. Despite advances in medicine and laboratory science, only a post-mortem can tell the full, and final, story.

By Marc Wortman

Shortly after lunch on a midsummer's day, Charles Slater felt ill. (His name and identifying details have been altered.) Complaining of indigestion, the 55-year-old administrator at a New Haven-area social services center headed home. Soon after, though, the pain became unbearable. He called for emergency medical service and paramedics arrived within five minutes, but he had already collapsed. The paramedics could find no pulse and tried to restart his heart and breathing. In the Yale-New Haven Hospital (YNHH) Emergency Department, physicians continued efforts to restore a heartbeat, but gained no more than a slight systolic fluttering. An hour after Slater telephoned for help, the doctor in charge declared him dead.

In most respects, the end of Slater's life, although sudden and unexpected, was identical to that of all others. A biological event of catastrophic proportions overwhelmed his body. In reviewing the medical records, John H. Sinard, M.D., PH.D., HS '93, FW '94, director of the autopsy service at YNHH, says that Slater had no serious apparent health problems before that day and kept himself in decent physical shape. A heart attack seemed the likely culprit, but the body holds many secrets. His family agreed to an autopsy. In this, the end of Slater's life stands out.

While every death is ultimately the same, in the eyes of those who deal with death for a living, "each death is different," says Sinard, an associate professor of pathology

With every autopsy, Art Bellanger, manager of the autopsy service at Yale-New Haven Hospital, draws a diagram of the body, noting scars, tattoos and previous injuries.



DAPHNE GEISMAR (2)



TOP An autopsy, says John Sinard, director of the autopsy service at Yale-New Haven Hospital, “is one of the few times you consider the whole patient and the whole disease process.”

ABOVE As manager of the autopsy service, Art Bellanger performs most autopsies, with the assistance of pathology residents.

and of ophthalmology and visual science. Every time a patient dies at YNHH, the family is asked to consider an autopsy, even when the cause of death is apparent. Very few consent. About 20 percent of patients who die at YNHH are autopsied. As in most teaching hospitals, that rate is significantly above the average for private and community hospitals, which is typically below 10 percent—and half of those are required for forensic or legal reasons. (In Connecticut, forensic autopsies are performed at the Office of the Chief Medical Examiner and, in the case of crime-related deaths, are often attended by representatives from the state police.)

Pathologists at Yale worry that even the hospital’s comparatively high rate of autopsies is barely sufficient—in the 1960s, more than 70 percent of YNHH patients were autopsied at death. (The Mayo Clinic, which has one of the highest rates in the nation, autopsies more than 35 percent of patients who die in its care.) “Around the 20 percent level is the minimum to provide a reasonable statistical basis for what is seen in the hospital,” contends Raymond Yesner, M.D., a professor emeritus of pathology who, at 91, continues to serve as a research scientist in the department. “Below that level, a hospital may not be monitoring care sufficiently, and you may see problems in quality control.”

Adds Rosemarie L. Fisher, M.D., HS ’75, professor of medicine and associate dean for graduate medical education, “From an internist’s point of view, I would like to see the rate higher, although we are probably higher than a lot of other institutions. Autopsies should be performed because they often contribute to knowledge about other illnesses that may be important for the care providers or the family to know about.”

With such low rates nationally, many pathologists are concerned that medical practices may be suffering. “If you get in the range of 10 to 15 percent these days, a hospital is doing very well,” says Kim A. Collins, M.D., who chairs the autopsy committee of the College of American Pathologists, the world’s largest organization of board-certified pathologists.

“Many people think we can diagnose everything before death,” says Collins, a professor of pathology and laboratory medicine at the Medical University of South Carolina. “But studies show that in close to half the cases, autopsies find something contributory or that the whole cause of death was different than physicians believed beforehand.” With investment in health care and biomedical

research based in part on mortality statistics, the evidentiary basis for that investment may now be distorted or even false. “Without enough autopsies,” Collins contends, “we really can’t be accurate with our epidemiological facts.”

In the age of genetic studies and imaging technologies, autopsies still provide a unique means for studying certain diseases and identifying previously unknown public health issues. Jon S. Morrow, PH.D., M.D. ’76, HS ’79, FW ’81, the Raymond Yesner Professor of Pathology, chair of pathology and professor of molecular, cellular and developmental biology, says: “Even to this day, autopsies are essential to the identification of a number of our latest scourges, like SARS, much of AIDS and other new diseases.” Moreover, he notes that even when no questions about cause of death may remain, an autopsy still provides a unique picture of a patient’s health and health care, which otherwise remains incomplete. “A patient is served by many different physicians,” he says. “The pathologist’s evaluation is where the data come together.” Those data can serve to improve teaching, research and medical care. He worries that the decline in the rate of autopsies may undermine the entire system. “We’re in danger of losing a critical piece of infrastructure.”

Nothing routine about death

Less than a day after Slater’s death, I don a head-to-toe jumpsuit and enter the autopsy room in the morgue in an extension to the Brady Memorial Laboratory. Half a dozen people cluster around Slater’s body, which lies on a long aluminum tray. Water flows continuously along a trough beneath the tray. A loud and powerful fan evacuates the air in the brightly lit room. With masks muffling our mouths and surgical caps pulled down over our ears, the echoing fan and splashing of the water make hearing difficult. Perhaps it is my own expectation, but all of us in the room seem intensely alert and attentive. There may be as many as five more autopsies performed this day, but the awesome presence of the dead and the seriousness of the investigation of death make nothing routine about any individual case.

An odor of bowels, cleansers and preservative chemicals—not quite sickening but enough to make a shower afterward a must—filters through the mask. Slater’s body extends straight except for his head, which is braced by a block beneath the neck and cocked upward. A white man,

his skin is yellow, waxy and splotched with patches of purple, except for the lower third of his back, which is bruised a deep burgundy. As I soon see, his blood has pooled there. He is tall, almost as long as the table, and appears to have been in pretty good shape for his age, with little fat bunched around his waist.

He still has most of his auburn hair, which is swept back from his forehead. His brown-green eyes stare straight into the harsh overhead spotlights. His elbows, bent rigidly, hold his forearms and hands a few inches off the table, as if he died while reaching for something with both hands.

He looks alive enough that it appears he could bend his elbows and push himself off the table when Arthur J. Belanger III, M.H.S., manager of the autopsy service, approaches Slater’s body and announces the present time, shortly after 1 p.m. Belanger is a jovial man with black-rim glasses and dark hair and a Navy tattoo on his thick forearm. He likes his work, enjoys explaining what he is doing and talks about it freely. With practiced swiftness, he picks up a scalpel and inserts the blade into Slater’s chest just beneath the top of the left collarbone. No blood flows from the wound.

A young college student considering a future as a pathology assistant flees the room. The others—two pathology residents and an aide—watch intently. Belanger swiftly slices downward and toward the center of the chest, cutting into the rib cage. He cuts at the tip of the right collarbone and continues down until the wound intersects with the other slice. In one swift, practiced cut, he sweeps straight down the abdomen to the top of the pelvic bone. With a pair of heavy-duty snips, he snaps the last resisting bones in the rib cage and hinges open Slater’s chest, exposing a sunken tangle of bluish gray, green and red organs. Belanger reaches inside Slater’s body cavity. He calls out his actions as he feels with his knife to cut all the central organs free of the arteries, muscle, thorax, bone, nerves and connective tissue holding them in place.

Much to learn from the dead

Death was once the greatest biological mystery, other than life itself. No longer. Medicine and health care have progressed to the point that, when a person dies, the physiological reasons are usually apparent. In some cases, the actual time of death becomes a matter of when the switch on the life-support machinery gets turned off.

The decline in autopsy rates reflects many factors, including costs (not borne by families of patients) of up to \$3,000 per autopsy and advances in diagnostic imaging and testing methods, endoscopic exploration and surgical interventions that make cause of death all but certain in most cases. Nonetheless, “As good as those ancillary studies are, we can’t diagnose everything pre-mortem,” insists Collins. “Even if you know the accurate cause of death, there’s still so much you can learn.” According to Sinard, who serves with Collins as vice chair of the College of American Pathologists’ autopsy committee, “It is one of the very few times you consider the whole patient and the whole disease process. It shows the physicians the extent of the disease process and the effectiveness of therapy for a patient. We may discover things that are entirely unexpected.” For the family and the doctor, it will usually answer any outstanding questions.

Given that so much is already known about a patient’s poor health and the causes of death, families often fail to grasp why an autopsy is needed at all. Many families resist what they perceive as a violation of the body after an often-arduous end of life. Perhaps as a result of all the forensic medicine series on television, many also think autopsies serve only to solve mysteries or to demonstrate a failure in their loved one’s health care. They worry that the request for an autopsy indicates a problem. Yet even when it reveals no surprises, says Sinard, an autopsy can be reassuring to the family. “We’re not policemen,” says Morrow. “We’re not looking for bad practices. We’re looking for accuracy and the quality of care. An autopsy almost always substantiates that the hospital and the physician did nothing wrong.”

How the news about a death is communicated can affect a family’s willingness to “help” medicine. “It’s the way it’s presented that matters,” Morrow says. “Physicians are often uncomfortable around death. They would often rather move on. The rates of autopsies, though, are higher when families are asked appropriately.” Few physicians ever bother to ask; most know little about autopsies or their value and have never attended one. And few medical schools require that their students attend autopsies. At Yale, medical students attend autopsies as part of the second-year pathology course, but as with all courses in the first two years, attendance is not mandatory. “It should be a routine part of a student’s education,” says Collins. “Everyone needs to know about it.”

Fisher, who directs Yale’s residency programs, notes that residents are less likely to observe an autopsy than in years past. “There used to be a 15 percent autopsy rate required for internal medicine residency program accreditation purposes,” she says. “That has just disappeared. Some programs now see only one or two autopsies a year. That’s a concern.”

Writing the last chapter

Even though all outward signs pointed to acute myocardial infarction—a sudden, devastating heart attack—as the cause of death, Charles Slater’s family agreed to an autopsy.

With two pathology residents looking on and occasionally assisting, Belanger cuts Slater’s organs—from the trachea to the testes—free of connective tissue and bone. Grasping the innards as a single mass in his arms, Belanger lifts the shiny, wet, shifting clump out of Slater’s body and sets it on a large white plastic surface that covers the other leg of the L-shaped autopsy table. The pathology residents then dissect the mass of organs, paring away the connective tissue, viscera and fat. Soon, the major organs are revealed. One by one those organs and major arteries are cut free.

Belanger and an assistant turn their attention to the head. After opening Slater’s skull cap with a vibrating saw, the gray brain is removed by cutting it loose from the brainstem and other soft-tissue attachments.

Meanwhile, the residents separate the removed organs, slicing the larger ones and examining the cut surfaces carefully for any signs of pathology. These are then placed on display trays for presentation to the attending pathologist. Some of the tissues, such as calcified coronary arteries, must be further prepared before they can be completely dissected.

Sinard enters the room and, with the pathology residents, reviews tissue from the organs. A resident presents the deceased’s clinical story, which is then discussed in the context of the pathological findings. Sinard and the residents select tissue for further, microscopic examination. Finally, the attending and the residents will review the case and determine the most likely sequence of events that led to Slater’s death. Slater, the deceased, has provided a valuable teaching tool. The residents participating in his autopsy would never otherwise have the chance to view a body’s organs whole, fresh and in context. They have also

benefited from viewing the consequences of biological and medical processes.

Their inspection shows that Slater's lungs were congested with blood, a telltale sign of heart failure. The heart itself had a slight grayish discoloration in the left ventricle wall, evidence of a sudden, devastating thirst for blood. To the touch, the pinkish white coronary arteries were brittle. Although it would take later decalcification to allow them to be sliced open, that appeared to be the "smoking gun," a single factor capable of causing death. Arteriosclerosis, by far the most common cause of sudden death in middle-aged men, was clearly present.

Belanger returns the remaining viscera to Slater's body cavity and replaces the crown of his skull. His assistant sews both shut. The pathology residents remain in the room, examining the organs and helping to catalog them for preservation. They have witnessed the conclusion of a life, from within a profession that pays special respect to the patient who has died.

"I tell my residents to handle with care," says Yesner. "What you are doing is writing the last chapter in somebody's life."

The death certificate is filled out, and Slater's body is released in condition for an open-casket funeral. A veteran, he will be buried three days later with military honors in a cemetery outside New Haven.

Help for the living

Two weeks later, the laboratory report is ready. In fact, one of the arteries had been entirely blocked by a fatty plaque that had dislodged from the artery wall, starving the heart of blood and sending it into lethal spasms as it strained for oxygen. The report also shows benign tumors developing in Slater's adrenal glands and intestine. The tumors had yet to cause symptoms, but had Slater lived, he would have encountered medical difficulties within a few years. They had not contributed to his death, but, says Sinard, "We are trying to catalog all of the disease processes in the patient." Armed with the report, his family members, who could themselves face similar conditions, will be in a position to take action. Such findings remind Collins that "there's so much you can learn about your own health by having an autopsy done on a deceased family member."

At Yale, tissue samples from every autopsy are frozen, placed in fixative solution or embedded in paraffin blocks for permanent storage. If questions should arise, tissue will be there for study—potentially avoiding exhuming a body. Longer term, the tissue may be used for teaching or research purposes. Yale possesses millions of tissue samples dating back to 1917, many of which have proven valuable for research, even decades after first being cataloged and stored. Autopsy-based research at Yale has led to a greater understanding of the worldwide flu pandemic of 1918-1919, resulted in descriptions of new forms of liver cancer and various pneumonias and expanded insights into the way blood reaches tumors. Today's research on Alzheimer's disease and other central nervous system disorders, which in most cases cannot be directly studied during a patient's lifetime, depends on autopsy material. "The speed of collecting and preserving the material is critical to the value of the specimen," says Morrow.

The national rate of autopsies has been in decline for decades. Since 1970 the Joint Commission on Accreditation of Healthcare Organizations has no longer required an autopsy rate of 20 percent to maintain accreditation. Morrow, Sinard, Collins and other autopsy pathologists have been trying to educate the medical community and the wider public about the need to reverse the trend. While there is no rate of autopsies considered minimally necessary by any national organization, "100 percent would be ideal," says Collins. "I wish we could have at least 20 percent nationally. Every family ought to be approached for the opportunity an autopsy offers them."

One day, a genetic factor may be found to underlie sudden cardiac death. Tissue collected in autopsies from patients such as Slater will almost certainly prove crucial in the development of new diagnostic methods and preventive therapies. The post-mortem picture of Slater's health may also prove directly beneficial to his own children and other relatives. "All of us will die," says Sinard. "That doesn't end what we can do for the living."

*Marc Wortman is a contributing editor of *Yale Medicine*.*



When animals sound a warning

Under the umbrella of a Yale center, ecologists and epidemiologists try to understand the not-always-felicitous interactions among humans, their environment and disease.

By Rhea Hirshman
Illustrations by Einat Peled

The native birds of Hawaii are vanishing. Of more than 100 species actively breeding on the islands when Capt. James Cook landed there in 1778, barely half remain and many of those are endangered. Having evolved in island isolation, with no mammalian predators, the birds were easy targets for alien rats—escapees from ships—which preyed on their eggs and their young. At the same time, bird habitats have been degraded by a range of human activities that date back more than 200 years, when cattle introduced to provide food for European settlers began to chew their way through the foliage.

But even though human activity has been damaging the Hawaiian bird population for centuries, the beginning of the population's drastic decline can be traced more precisely to 1826, when the encroachers were not bulldozers flattening delicate ecosystems or pesticides spread for agribusiness (those threats came later), but mosquitoes brought by a whaling ship from Mexico. Two weeks after the ship left, after taking on water and washing out its casks, locals were complaining to missionaries about a new kind of fly that flew at night and buzzed.

“There had been no mosquitoes in Hawaii before then,” says Stephen C. Stearns, PH.D., “and these mosquitoes could transmit malaria.” Not only did avian malaria decimate the

When Capt. James Cook first visited Hawaii in 1778, he brought animals previously unknown on the islands—and against which native species had no defenses. The ships that followed brought goats, cattle, sheep and mosquitoes, altering the environment in unforeseen ways.





native bird population, Stearns notes, “but when humans brought yellow fever to Hawaii, the mosquitoes were there to transmit the human disease as well.”

The interplay among human behavior, human health and disease, animal behavior and health and the ecology of the planet is the foundation of the activities of the new Center for EcoEpidemiology, which was established as part of the Yale Institute for Biospheric Studies and began operation on July 1 last year. Stearns, the Edward P. Bass Professor of Ecology and Evolutionary Biology and chair of ecology and evolutionary biology, is one of more than a dozen Yale faculty affiliated with the center. A specialist in the life history consequences of infections and disease, co-author of a widely used textbook on evolution and the founding editor of the *Journal of Evolutionary Biology*, Stearns calls the center “an important cross-disciplinary effort to both understand and anticipate the consequences of humanity’s interacting with the environment.”

Faculty from the School of Medicine (departments of Internal Medicine and Epidemiology and Public Health), the School of Forestry and Environmental Studies (FES), the Graduate School of Arts and Sciences and Yale’s Department of Ecology and Evolutionary Biology are among those participating in center activities. The center’s director, Durland Fish, P.H.D., notes that—through fostering the creation of new undergraduate and graduate courses, hosting seminars and symposia, coordinating Yale’s existing cross-disciplinary curricula and helping to develop an interdisciplinary doctoral program in epidemiology and ecology/environmental science—it will be addressing two main themes.

“The first,” Fish says, “is how do we integrate environmental and ecological sciences into infectious disease epidemiology? The focus in combating diseases has traditionally been to concentrate on individual humans or discrete groups of humans—for instance, by developing diagnostic techniques or vaccines. But many important human pathogens, whether transmitted human to human, animal to human or vector to human, originate in the environment. The risks of incurring or transmitting infection have everything to do with what happens in the environment.” Fish adds, “I view infectious diseases as environmental threats—measurable and predictable. So we want to look at how to get the ecological sciences as equal participants in understanding and combating infectious diseases.”

A professor of epidemiology (microbial diseases) at the School of Public Health (EPH) and principal investigator of the Centers for Disease Control and Prevention’s Fellowship Training Program in vector-borne diseases, Fish notes that he had experienced a “lack of communication between ecology and epidemiology” throughout his career. “I studied the ecology—the abundance and distribution—of insect-borne pathogens. There wasn’t much support for this kind of work, because in the 1960s we thought we had conquered all kinds of infectious diseases with drugs and vaccines.”

However, Fish points out, diseases thought to be controlled or eliminated have re-emerged, while “new” infections including Lyme disease and West Nile virus have also surfaced. Suburbs that encroach on once-natural areas bring humans in closer contact with deer and the deer ticks that carry Lyme disease. In parts of Central and South America, a decade-long pandemic of dengue fever is attributable to an increase in the number of items such as tires and cans—used as containers or left as garbage—that hold the standing water that becomes a breeding ground for mosquitoes. In these and a wide range of other instances, zoonotic diseases—those caused by infectious agents that can be transmitted between (or are shared by) animals and humans—have everything to do with environmental disturbance, human population growth and the speed with which people, animals, plants and materials are transported around the world.

The second theme of the center, Fish says, is “getting the tools of human medical science into the hands of those studying disease ecology and environmental health.” He notes, for instance, that David K. Skelly, P.H.D., another faculty member affiliated with the center, is using ultrasound technology originally developed as a diagnostic tool for humans to study parasitic cysts in frogs. Amphibians, he notes, have been central to the development of biological knowledge and have become icons for environmental decline.

“We can learn a lot about human health by looking at nonhuman systems, and the development of the field of ecoepidemiology is a recognition of that,” says Skelly, a professor of ecology at FES and of ecology and evolutionary biology, and a 2003 recipient of a Guggenheim fellowship to write a book on amphibians aimed at the general public. “Animals and plants can be sentinels—whether we’re dealing with risks that are infectious or chemical. What sorts of environmental conditions are conducive to disease? How



does the exposure of a frog in a pond to infection or toxins or pollutants translate into possible human exposure, and what are the effects of that exposure? Our message as scientists should not be only about risks to humans. But if we are modifying our environment so that reptiles are becoming hermaphrodites, we have to ask if there is a relationship to the decrease we're seeing in human male sperm counts."

While Skelly uses tools of biomedical science in his work as an ecologist, he talks in turn about the relevance of ecological tools and methods to medical research. "As an ecologist, I know that the emerging field of disease ecology shows us a discernible relationship between infectious agents and species distribution and abundance." Skelly says that the tools of ecology, including field experimentation (going out into the environment where infection happens, modifying some part of the natural world and comparing it to a control location), "are now spreading into the biomedical world—medical researchers are building models and testing them in nature, taking the study of disease outside the laboratory and looking at the environmental contexts of disease and infection."

Using Lyme disease as an example of changing perspectives on managing infection, Skelly asks, "Can we decrease Lyme disease risk by intervening with nonhuman hosts?"

Fish, who has worked on Lyme disease "since the beginning," also talks about taking a different approach. "An ecological perspective to preventing Lyme or any other vector-borne disease involves thinking about how populations are regulated by nature and how we can work within the natural environment to reduce the presence of disease vectors."

He points out that in the case of Lyme disease, reforestation of the Northeast has caused changes in the population density and distribution of the white-tailed deer and, correspondingly, its natural parasite, the deer tick. These changes have caused a Lyme disease epidemic as humans have increasingly come into contact with ticks infected with Lyme disease bacteria. "We did an experiment—using the vaccine originally developed for humans, we vaccinated mice in the woods outside of New Haven. Over the next several years, we found fewer infected ticks. While human vaccination turned out not to be an effective defense against Lyme disease, this research path is promising." The point, Fish emphasizes, "is that there is a range of options for us to work with."

From his discipline, Stearns also notes the importance of looking at "ecological context," which he describes as standard evolutionary thinking. "Every organism 'wants' to survive," he says. "We can't really understand the development of virulence or resistance or the emergence of diseases like Ebola or SARS or AIDS unless we look at that ecological context, one that humanity has often affected."

To illustrate his point, Stearns tells what he calls a cautionary medical tale—the consequences of the spread of a cattle disease (rinderpest) into Africa. Rinderpest first evolved in Eurasia, entering Africa either with General Charles Gordon's attempt to lift the siege of Khartoum in 1885 or with the Italian invasion of Ethiopia in 1895. In Africa rinderpest encountered a continent with no evolutionary experience of—or immunity to—the disease. "The rinderpest virus spread rapidly all the way south through Africa, reducing native herds of hoofed animals down to about 1 percent of their former levels," says Stearns. "Lions, whose prey were dying off, began eating people."

"In true ecological fashion," Stearns says, the effects of these events on the human population were significant. Without the grazing animals, bushes grew up along creeks and river beds—and created ideal environments for tsetse flies. "So when people tried to move back after the virus had gone through," Stearns continues, "they encountered sleeping sickness." Now, decades later, those areas that experienced a high incidence of sleeping sickness are the national parks of Africa, because giraffes and antelopes and many other wild animals are not affected by sleeping sickness, which kills both cattle and humans.

"The interactions between predators, prey, pathogens, vectors and vegetation reshaped the human ecology of a continent for a century," Stearns says. "No one could have predicted this when some sick cows came along with an invading army into northern Africa."

Looking beyond the immediate and the obvious and paying attention to the possibility of the unpredictable are central to the interdisciplinary mission of the Center for EcoEpidemiology. The overall goal is to develop an innovative curriculum among the participating schools and departments to provide training that cannot be obtained at any other American academic institution. "I'm also hoping to see more emphasis on prevention in a much more global way. We want all sorts of new ideas to emerge," says Fish, "and there is a lot of excitement about what we're doing. When the creation of the center was announced I was inundated with e-mails and phone calls from people wanting to be involved or to know more."

A listing of just some of the topics under consideration for the center's fall seminars—the impact of global warming on infectious disease, biodiversity, environmental change, wildlife as sentinels for environmental hazards, health implications of fossil fuel use, potential bioterrorism threats to the environment—illustrates the range of interests of participants and the possibilities that the center holds. Stearns envisions the center as "a place to train a new generation of graduate students to observe the world in new ways and come up with syntheses that my generation was not trained to be able to see." Skelly adds, "We want to train people who are oblivious to disciplinary boundaries. Once faculty and students from different disciplines start talking to each other, there's no telling what can happen."

For more information about the Yale Institute for Biospheric Studies Center for EcoEpidemiology, and a list of upcoming events and courses, check the center's website at <http://www.biology.yale.edu/oib/resources/yibs.htm>.

Rhea Hirshman is a freelance writer in New Haven.



Rigging the roulette wheel to slow the spread of viruses

Avian flu virus is not new. All the influenza strains that affect people have avian origins—including the virus that caused the 1918-1919 influenza pandemic, according to Durland Fish, PH.D., professor of epidemiology. That outbreak killed at least half a million people in the United States and more than 30 million worldwide. As with such other "emerging" diseases as Ebola hemorrhagic fever, Lyme disease and severe acute respiratory syndrome, or SARS, what is "new" about avian flu is a heightened awareness of the role of other species in the development of this human health hazard, says Fish. That makes it a perfect case study for the new center Fish directs, the Center for EcoEpidemiology, part of the Yale Institute for Biospheric Studies. The center's purpose is to bring together experts in ecology and epidemiology in areas where their studies intersect.

Fish highlighted one such intersection in a talk at a conference on campus last May, "Ethical Aspects of Avian Influenza Pandemic Preparedness, Part 1: Vaccines," when he discussed the necessity of focusing more resources on understanding how the virus evolves and functions in wildlife populations so that we can keep it from developing into a strain transmissible to humans.

Of the numerous strains of the influenza virus, of most concern is the H5N1 strain. "A common scenario is that avian viruses in wild-bird populations are transmitted to domestic birds or sometimes to pigs. New strains can evolve when animals are in proximity to each other," Fish says. This process is known as "recombining." Although humans have developed some

immunity to various influenza genotypes through exposure, they would be highly susceptible to the new strain were it to become widespread in the human population.

What could make that happen? Fish says that we do not know why some strains jump the species barrier to humans and others do not. "We do know," he says, "that the H5N1 strain recombined in domestic animals and is now back in the wildlife population. We saw the first human cases in the late 1990s. When several people in Southeast Asia died of a previously unknown influenza virus, the virus was studied and we now know it as H5N1."

A pandemic occurs when a virus introduced into the human population through another species moves from person to person. Rather than relying on the wholesale destruction of infected and susceptible bird populations, or pouring resources into developing a human vaccine (he notes the impracticality of vaccinating billions of people quickly), Fish suggests other ways to keep a pandemic at bay.

"The first," he says, "is to vaccinate carrier species against viral genotypes with pandemic potential by developing oral vaccines that can be distributed to wild birds through feed." Another approach would involve the introduction of a variation of the virus that produces a milder form of the infection but still maintains itself in appropriate bird populations, thus rendering the birds immune to pandemic genotypes.

Fish would like to see greater cooperation between the disciplines of ecology and epidemiology. "We should preserve wildlife, while at the same time figuring out how to keep it from being a threat. If we can buy time and learn more about the evolution of viruses in nature, we can rig the roulette wheel rather than just waiting for it to turn."

—R.H.



Making a better doctor, and better patients

After Hurricane Katrina, a day at a convention center in Texas provided lessons in dignity and sympathy.

What exactly did I think I was getting myself into? As I approached the Austin Convention Center's loading dock, which was swarming with people, it felt like an enormous hospital—a hospital not only for the sick but also for the weary-hearted. I had come simply to see whether I could help other evacuees; I didn't expect them to teach me a lesson in clinical medicine.

I had been living in New Orleans for only six days before leaving town. I never got the chance to start at Tulane's School of Public Health and Tropical Medicine. Along with my landlord and his family, I rode out Hurricane Katrina in Houma, La., a predominantly Cajun town southwest of New Orleans. I awoke the morning after the storm, surprised that I'd slept through the brunt of it. Slivers of light invaded my room through boarded-up shutters. Lawn furniture, branches, leaves and other debris lay strewn across the backyard, and the gusting wind carried an eerie chill. What next? I asked myself.

When I heard of the devastation of New Orleans, I left my refuge to stay with friends in Austin, Texas. I volunteered to help at the convention center, which housed 4,000 evacuees: some riding the high of a miraculous escape, others succumbing to depression after seeing their homes and livelihoods swept away. All, however, were emotionally fragile.

I discovered their vulnerability while distributing toiletries and clothing to people lined up for showers. Grown women reluctantly asked me for clean underwear. They'd make a request, and I would search for the right size. Sometimes I had to turn back for a larger size, embarrassing the woman I was serving. One woman asked me for a feminine hygiene product and I wasn't sure what she needed. I felt flustered and she told me to forget the request. As she walked away I knew I'd seriously messed up.

I did better when my job was to help elderly and disabled men at the showers. As I wheeled one man into the changing room, he recounted the story of a treacherous week. Together we peeled off his clothing one piece at a time: His legs wobbled as he hovered above the wheelchair. His soiled underwear dropped to his ankles, and I tossed the garment in the trash heap. Steam from the showers and the midday Texas sun cooked the air inside the shower room; the smell was nauseating. I had to fight the urge to rush outside for a breath of fresh air. The man's eyes showed me his underlying feelings of humiliation. I knew that registering my revulsion would only make him feel worse. So I held back my feelings and told him how wonderful his shower would feel, hot water hitting his back for the first time in 10 days. Ahh.

It doesn't take much to make a patient feel afraid or ashamed. Sometimes a reflexive shudder will do it. Or maybe a grimace or an unthinking remark. The consequences are serious. Once people are made to feel inferior or disgusting, they shut down. They're not as likely to be open, honest or compliant.

I often thought about Austin after finding a home for the fall at the Yale School of Public Health. I began using my experiences there as a lens for understanding my classes. In the health policy course, for instance, Mark J. Schlessinger, PH.D., professor of public health, explained how stigma can compromise the quality of health care. Patients with a stigmatized illness, he explained, are less likely to seek care. Furthermore, he told us, physicians are more likely to sidestep critical issues related to conditions that carry a stigma. My mind reeled back to the Austin Convention Center and I understood that when I embarrassed the woman who needed sanitary products, I had unintentionally denied her appropriate care. Later, my ability to overcome my discomfort with the man in the shower allowed me to help him without compromising his dignity.

I didn't work in a hospital, help out in an ER or scrub for surgery, but in Austin I learned something about clinical medicine. I have promised myself that when I become a physician, I will remember the lessons the evacuees taught me about the importance of unabashed sympathy. I think those lessons will make me a better doctor and help my patients to be better patients.

David Grew, of West Hartford, Conn., returned to New Orleans this spring to complete his public health studies after spending the fall semester at Yale. He hopes to enter medical school in August.

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Pietro De Camilli



Stephen Strittmatter



Ira Mellman

New center to focus on neuroscience and brain disorders

The School of Medicine has launched a new interdepartmental program, Cellular Neuroscience, Neurodegeneration and Repair (CNNR), to be led by PIETRO DE CAMILLI, M.D., FW '79, the Eugene Higgins Professor of Cell Biology, and STEPHEN M. STRITTMATTER, M.D., PH.D., the Vincent Coates Professor of Neurology and professor of neurobiology.

The CNNR will build on Yale's tradition of excellence in the neurosciences through the departments of neurobiology, molecular and cellular physiology, pharmacology, cell biology, psychiatry, neurosurgery, neurology and others, and the Child Study Center. Its goal is to foster cutting-edge basic research in cellular and molecular neuroscience, promote research on neurodegeneration and repair, translate scientific insights into therapeutic strategies to prevent or delay neuronal loss, and facilitate neural repair and restoration of function. This interdisciplinary program could have a significant impact on diseases such as Alzheimer's and Parkinson's, amyotrophic lateral sclerosis and multiple sclerosis, as well as diseases related to *polyglutamine expansion*, such as Huntington's.

De Camilli's pioneering work on synaptic vesicles, the intracellular packets that deliver neurotransmitters into the synapse, could advance the understanding of brain function, as well as the causes of Alzheimer's, Parkinson's and other diseases.

Strittmatter's identification of Nogo, a protein that blocks the regeneration of axons, has opened promising avenues in the search

for therapies to repair the adult nervous system after injury, and has given new hope to those who suffer from spinal cord injuries, stroke and neurodegenerative disorders such as Alzheimer's.

De Camilli and Strittmatter, who will retain their appointments in cell biology and neurology, respectively, will recruit up to seven new scientists for the CNNR. The searches will be carried out in collaboration with colleagues in the basic-science and clinical departments who work in the neurosciences, and the new recruits will have primary appointments in existing departments. In addition, the CNNR will provide a scientific home for more than 100 neuroscientists who now work across the Yale campus, sparking greater interactions and enhancing the scientific environment.

European group elects cell biologist as foreign member

IRA MELLMAN, PH.D. '78, chair and Sterling Professor of Cell Biology, is one of three American scientists elected as foreign members of the European Molecular Biology Organization (EMBO) at its annual meeting in Warsaw, Poland, last October. EMBO membership is a lifelong honor, and scientists are elected on the basis of proven excellence in research. Among its members are some of Europe's leading researchers, including 38 Nobel laureates. EMBO was established in 1964 to create a central molecular biology laboratory and a network that would enhance interactions among European laboratories. Currently there are more than 1,200 EMBO members in Europe, and only 100 investigators outside of Europe have been named as associate members.

"It is a real honor to be one of the very few U.S. scientists to be recognized by our most distinguished European colleagues by election to EMBO membership," said Mellman. "Science is truly an international endeavor, and I certainly plan to use this connection to further scientific exchange at all levels."

Mellman uses a combination of biochemical, genetic and imaging methods to understand complex functions of cell biology. His work has revealed basic biological mechanisms that regulate immune responses, particularly how dendritic cells initiate and control all antigen-specific immune responses. Another area of his research involves cell polarity and asymmetry and the molecular mechanisms that sort, target and transport cell membrane compo-

nents to appropriate membrane locations in different types of cells.

Mellman joined the Yale faculty in 1981 after completing his undergraduate training at Oberlin College, receiving his doctorate in human genetics from Yale in 1978 and beginning his academic career at Rockefeller University. From 1997 to 2001 he served as founding director of the Combined Graduate Program in Biological and Biomedical Sciences.

Mellman, who holds a joint appointment in the Department of Immunobiology, is an affiliate member of the Ludwig Institute for Cancer Research. He was named scientific director of the Yale Comprehensive Cancer Center in 2004. He is a fellow of the American Academy of Arts and Sciences and the Leukemia & Lymphoma Society, and he has received a Swebilius Award, the President's Research Development Award (Leukemia & Lymphoma Society) and the Yale Science and Engineering Society Medal.

**Margaret Bia**

Margaret J. Bia, M.D., professor of medicine, received the George F. Thornton Award at the annual meeting of the Connecticut chapter of the American College of Physicians in October. The award is given annually for outstanding contributions to medical education.

Linda K. Bockenstedt, M.D., the Harold W. Jockers Associate Professor of Medicine, has been named director for professional development and equity at the medical school. In this new position Bockenstedt will be responsible for creating programs to support the academic development of all faculty members and to encourage the growth of a diverse faculty body at the school. A special focus will be on the needs of women and underrepresented minorities.

Rosemarie L. Fisher, M.D., HS '75, associate dean for graduate medical education, has won the 2006 Courage to Lead Award from the Accreditation Council for Graduate Medical Education. The award honors designated institutional officials who have demonstrated excellence in overseeing residency programs at their sponsoring institutions. Designated institutional officials are responsible for all graduate medical education programs in a teaching hospital, community hospital or other type of institution that sponsors residency programs. Fisher oversees residency programs at Yale-New Haven Hospital.

Nora E. Groce, PH.D., associate professor of public health (global health) and anthropology, chaired UNICEF's Thematic Group on Violence Against

**Rosemarie Fisher****Nora Groce**

Disabled Children, which in November issued a report that is part of a larger report on violence against children. The study is a collaborative effort by the United Nations Secretary General's Office, the World Health Organization and UNICEF and is a follow-up to a 1999 U.N. study on children and armed conflict. The new report is intended to bring the issue of violence against children to the attention of policy-makers, governments and civil society around the globe. Corrie E. Paeglow, a graduate student in the Global Health Division at the School of Public Health, served as research associate on the project.

Sharon L. Kagan, D.ED., professor (adjunct) in the Child Study Center, has become the first woman to win three of the nation's most prestigious education awards. Kagan, a leader in early childhood education, won the 2005 Harold W. McGraw Jr. Prize in Education, the 2005 James Bryant Conant Award from the Education Commission of the States and the 2004 Distinguished Service Award from the Council of Chief State School Officers.

Zeev N. Kain, M.D., M.B.A., HS '92, FW '93, professor of anesthesiology, pediatrics and child psychiatry and vice chair of anesthesiology, has been appointed to the editorial board of the *Journal*

**Zeev Kain****Christopher van Dyck**

of Pediatric Psychology, the first anesthesiologist to hold this honor. Kain, who is also a member of the editorial boards of *Anesthesiology* and *Pediatrics*, is an international expert in the area of perioperative behavioral and physiological stress.

Each year the graduating class honors its teacher of the year with the Francis Gilman Blake Award, but this year the other three classes chose their own teachers of the year. The Class of 2006 honored **Laura R. Ment, M.D.**, professor of pediatrics and neurology, and **I. George Miller, M.D.**, the John F. Enders Professor of Pediatrics and professor of epidemiology and of molecular biophysics and biochemistry. The Class of 2007 selected **Margaret J. Bia, M.D.**, professor of medicine, and the Class of 2008 named **James D. Jamieson, M.D., PH.D.**, professor of cell biology and biology, and **Shanta E. Kapadia, M.D.**, lecturer in surgery (gross anatomy).

Jennifer P. Ruger, PH.D., M.S.C., assistant professor in the Global Health Division of the Department of Epidemiology and Public Health, was awarded the 2005 Labelle Lectureship in Health Services Research, given annually by McMaster University in Ontario, Canada. The lectureship is given to a young investigator who has a background in health economics and research that spans disciplines, and who challenges existing methods or accepted ideas in the health services community. Ruger's lecture, "Health and Global Governance: What's Justice Got to Do With It?," was presented on October 19.

**Agnès Vignery**

Christopher H. van Dyck, M.D., FW '91, associate professor of psychiatry and neurobiology and director of the Alzheimer's Research Unit at the School of Medicine, was among six honorees at the "Removing the Mask" gala celebration held in October at the Omni New Haven Hotel. The mask motif is a metaphor for the devastating loss of identity and cognition caused by Alzheimer's disease. Gov. M. Jodi Rell was the event's honorary chair.

Agnès M. Vignery, PH.D., D.D.S., associate professor of orthopaedics and rehabilitation, has been named Yale-Pfizer Global Discovery Visiting Professor for 2005. Vignery, whose research focuses on the developmental and reconstructive processes of bone, will serve as a consultant at Pfizer's Groton (Conn.) laboratories. She will conduct collaborative research while gaining practical knowledge of the drug discovery and development process through interactions with the project teams. The program, which offers a 12-week position for one Yale faculty member to consult and do research on-site at Pfizer Global Research and Development, strengthens Yale-Pfizer alliances and provides Yale faculty with new collaborations and a better understanding of the pharmaceutical industry.

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JOHN CURTIS (3)

PA grads urged to keep learning

Only through constant learning can health professionals keep up with medicine.

At their Commencement in September the 29 members of the Physician Associate Program's Class of 2005 heard words of encouragement from Joxel Garcia, M.D., M.B.A., former commissioner of public health for the state of Connecticut and current deputy director of the Pan American Health Organization.

"These are exciting times to be in the health care field," Garcia said, citing new technology and new medical discoveries. But this day, he continued, would be a benchmark in the new graduates' careers. "Anything you do from today on is going to have an impact five, 10, 20 years from now. Today is all about you and how you are going to fulfill yourself as a person. Just make sure you do what you love to do. Never compromise yourself for things that are going to be short-lived or are not going to make you happy."

His closing admonition to the graduates was to "keep learning. ... If you are not learning you won't be able to adapt yourself ... to the new realities of life."

In keeping with Garcia's advice, Robert J. Alpern, M.D., dean of the School of Medicine and Ensign Professor of Medicine, said, "Medicine is changing so fast that what you've learned will probably be completely out of date five years from now." Noting the unequalled academic achievements of the Class of 2005, he said, "People will look to you for leadership—not just to

practice health care, but to lead it."

This year's Didactic Instructor Award for dedication and excellence in the classroom went to J.G. Collins, PH.D., professor of anesthesiology and lecturer in pharmacology. David Spiro, M.D., M.P.H., assistant professor of pediatrics (emergency medicine), and John Roney, PA-C, lecturer in pediatrics, shared the Clinical Instructor's Award, given to recognize exemplary teaching at a clinical rotation site. John P. Hayslett, M.D., HS '65, professor of medicine (nephrology) and of obstetrics, gynecology and reproductive sciences, received the Jack Cole Society Award for contributions in support of the physician associate profession.

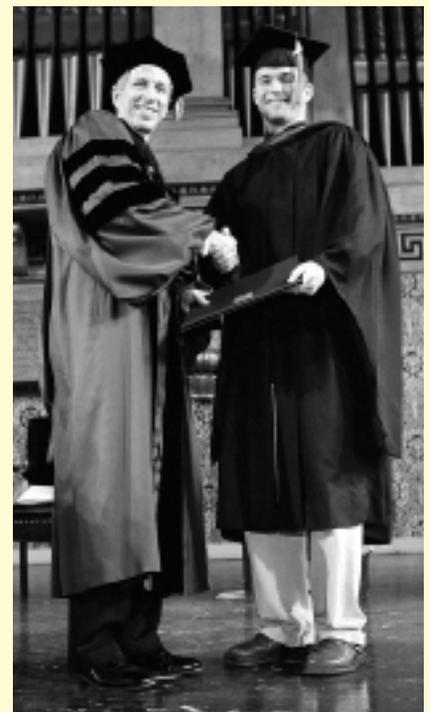
—John Curtis



TOP Joxel Garcia, former commissioner of health for the state of Connecticut and current deputy director of the Pan American Health Organization, was the Commencement speaker.

ABOVE Kristin Noell-Casey, Susanna Cho, Laura Desilets and Jeff Donnelly applauded speakers at the ceremony.

RIGHT Daniel Walsh received his diploma from Dean Robert Alpern.





Proposing a new paradigm as international health hits close to home

Each October, students in medicine, nursing and public health present their findings from a summer of research abroad at the Committee on International Health Symposium Poster Session and Reception. But last year Hurricane Katrina cast a shadow as Curtis L. Patton, PH.D., director of International Medical Studies and professor of epidemiology, suggested that health issues once thought to occur only in the developing world have emerged in this country.

"The United States is clearly part of the globe," Patton said. "We have all thought of ourselves as separate and distinct and immune from disasters. We should seriously consider having students who want to do international health, do international health in the United States. Problems we have had this past fall suggest that there are opportunities to do in the United States the kind of work that is truly international."

Three students made oral presentations at the symposium. Sayaka Ogata, a nursing student, described the integration of HIV/AIDS services with family planning in rural China. Public health student Vidya Angundi studied placental malaria in western Kenya. The placenta, she noted, is susceptible to the most severe form of malaria. Carolyn Graeber, a medical student, measured central corneal thickness, a gauge of intraocular pressure that is a factor for the development of glaucoma, in Puerto Rico.

—J.C.



Still going strong—Hunger and Homelessness Auction nets \$32,000 for local groups

Thirteen years ago a second-year student asked his classmates to join him in a fund-raising activity in which he'd participated as an undergraduate at Haverford College. Now that activity, the Hunger and Homelessness Auction, has become a tradition at the medical school, growing from a one-day affair to a flurry of activities spread over several days, including a football game, a dinner and a silent auction with hundreds of offerings. This year the auction raised \$32,225 for seven organizations in New Haven.

The first auction in 1994 netted \$3,500 and had far fewer activities, recalled Jeffrey A. Meyerhardt, M.D. '97, who organized it. "The silent auction," he said, "was just two tables." Meyerhardt, now at Harvard Medical School and the Dana-Farber Cancer Institute, returned to Yale in November to relate the history of the auction. Some things don't change, he said in a subsequent interview. William B. Stewart, PH.D., associate professor of anatomy, is still auctioning off his trademark bowtie, and Frank J. Bia, M.D., M.P.H., FW '79, professor of medicine and laboratory medicine, is still called upon, as he was this year, to serve as an auctioneer. Richard Belitsky, M.D., associate professor of psychiatry, shared this year's auctioneering chores.

Items on the block included, as in past years, weekends in faculty vacation homes, meals at restaurants or faculty homes, baby-sitting services, rides in planes and on yachts, various

FAR LEFT Sayaka Ogata, a nursing student, examined how family planning workers in the Chinese province of Henan integrated HIV/AIDS services into their work.

LEFT First-year medical student Matty Vestal and his girlfriend, Sarah Hunt, looked over items up for auction.

types of lessons (language, sports, music, art) and lots and lots of food items. Perhaps the most unusual offering, with a starting price of 50 cents, came from second-year student Maggie Hatcher: "Former rugby champ will tackle you three times this year when you least expect it." Her offer netted \$50 from a bidder who preferred to remain anonymous.

—J.C.



Medical student receives psychiatry fellowship

Second-year medical student **MALLIKA LAKSHMI MENDU** has received a 2005 Jeanne Spurlock Minority Medical Student Clinical Fellowship in Child and Adolescent Psychiatry from the American Academy of Child and Adolescent Psychiatry. The fellowship provides minority medical students with opportunities to work with outstanding child and adolescent psychiatrist mentors. James F. Leckman, M.D., the Neison Harris Professor of Child Psychiatry in the Child Study Center and professor of pediatrics, will serve as her mentor.

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Sauces, sunflowers and letters home

An Air Force surgeon in Iraq talks of his soldiers, Iraqi families and his feelings about the war.

Christopher P. Coppola, M.D., HS '01, didn't get much sleep during the four months he spent as a surgeon at Balad Air Base about 40 miles north of Baghdad.

The injured would arrive without warning. For instance, soon after Coppola, an Air Force major in the 332nd Expeditionary Medical Group, arrived in January 2005, insurgents attacked a police graduation ceremony in the nearby city of Baqubah. Six surgical teams, including Coppola's, rushed to Balad's tent-and-shipping-crate hospital as one helicopter after another delivered gruesomely injured policemen.

On other days—and nights—the burned and wounded who kept Coppola from his rest were American troops, Iraqi National Guard soldiers, children caught in the cross-fire and men and women hurt in fights or accidents on the base that housed 25,000 American troops and 7,000 civilian employees of Halliburton subsidiary KBR. Frequent mortar attacks led soldiers to nickname the base "Mortaritaville," Coppola said, but many of the insurgents' decades-old shells failed to detonate. "When they did go off, they would startle me and I usually couldn't sleep for the rest of the night," he said.

Coppola did relax a bit when the violence abated. On those days, his only responsibilities were scheduled procedures—inserting stomach tubes,

cleaning wounds. But going back to his hooch to catch up on sleep provided the unwelcome opportunity to reflect on his situation. "When you're cutting off someone's leg, you just do it, because they're going to die if you don't," Coppola explained in an interview from Lackland Air Force Base near San Antonio, Texas, where he now works. "When you have nothing to do, you start thinking about it. So I couldn't sleep."

The 37-year-old Coppola used some of his restless nights to write long letters to family and friends. His wife, Meredith, has assembled them in a self-published book, *Made a Difference for That One: A Surgeon's Letters Home From Iraq*.

Coppola described in the letters how he distracted himself from missing Meredith and their three sons and from the despair he felt about the suffering surrounding him. He ran for exercise, always wearing 35 pounds of armor and a helmet, occasionally waving to shepherds just beyond the fence; planted cilantro and sunflowers in the sandbags banked against his sleeping quarters; and earned modest fame in a moustache-growing competition. To make edible such meals as "tan stuff over rice," Coppola assembled an arsenal of sauces. In March, for instance, faced with an entree of "meat chunks ... diluted with unmentionable adulterants," he saluted St. Patrick's Day by dousing it with Goodall's of Dublin Irish Steak Sauce.

Coppola owed the Air Force six years of service in exchange for stipends while training in pediatric surgery at Children's National Medical Center and for medical school tuition at Johns

While stationed in Iraq, surgeon Christopher Coppola used an assortment of spices to liven up meals full of "unmentionable adulterants."



CHRISTOPHER COPPOLA

Hopkins. He did his general surgery residency at Yale, serving as chief resident in 2000-2001. Although he worked as an all-purpose trauma surgeon at Balad, word got around that he was a pediatric surgeon, and Iraqis brought their children to him for care: a girl with kidney failure, a boy with a prolapsed bowel. Coppola also treated children hurt in the war, including two sisters burned when their house was fire-bombed. One child recovered, but the other died. Soon after, Coppola discovered that he had unknowingly saved the life of the man who threw the bomb. "I instantly conceived of a variety of ways I could have meted justice on him with my own hands," Coppola wrote. "I've taken care of drunks who have plowed into a family of five on the highway, in the bed next to the parents whose children were



killed in the crash, but nothing prior had been as difficult as this. I was thankful I didn't know who he was while he was here."

Coppola recalled becoming injured to the carnage, only to be shocked yet again. "You feel like you've seen it all, but you haven't. There's always something worse around the corner."

Coppola opposes the war. "I want out of there, yesterday. I can't see how any father or any doctor could feel differently." And yet the work itself was rewarding. In Texas, Coppola knows that if he does not care for a patient, someone else will. In Iraq, he said, "I had the privilege of feeling that if I wasn't there, the person would probably die." And although he believes the war hurts American interests more than it helps, "If there were Americans shot at, that was the place I had to be. Trying to get those guys and women home to their families is probably the most rewarding thing I'll ever do."

Coppola expects to be sent back to Iraq this September.

—Cathy Shufro

Made a Difference for That One is sold by online booksellers and also on www.iuniverse.com. Profits go to Fisher House Foundation, which provides housing for family members of military personnel getting treatment at military medical centers.

A long, full and active life—keeping fit and taking on lots of jobs

"The trouble with retirement is that you never get a day off," is a saying quite familiar to **Henry E. Markley, M.D.** '43. At 87, Markley went into full-time retirement when Greenwich Hospital's Home Care/Hospice Program, where he worked as part-time medical director, closed in September 2004. Although he bristles at the closing of the program, which served up to 300 patients, he has no plans to slow down. An avid tennis and golf player, he continues to exercise up to an hour and a half each day, a testament to the notion that a healthy lifestyle leads to a long and healthy life.

Markley's ties to the hospital's home care program go back half a century, when an anonymous donation enabled the hospital to set up a pilot home care study for chronically ill patients who often required lengthy hospital stays. The only nursing home in Greenwich had a long waiting list, so there was a dire need for alternate long-term care. After visiting Montefiore Hospital's home care program in New York, Markley helped set up the Greenwich service, which initially accommodated only 10 patients. "By the seat of our pants we built up the program," he said. "We were a pioneer service." After a year, in 1956, the medical staff voted unanimously to request that the hospital make home care a department, and Markley continued as medical director for almost 50 years. The program was recognized across the state, serving patients from Greenwich and its surrounding communities.

Markley's medical career began with a lingering doubt. When he applied to the School of Medicine in 1939 he had little hope of being accepted. He was a top student at Penn State, but most medical schools then had an unspoken quota limiting Jews to 10 percent of any given class. One of his Jewish classmates from Penn State had already been accepted at Yale, and Markley thought it unlikely that, with a class of only 48 students, the school would accept two Jewish students from the same college. Much to his surprise, however, he entered the medical school with the Class of '43. After being drafted, he joined the Reserve so that he could postpone his Army service until he graduated. The war ended not long after he went on active service, and following an internship at Philadelphia General Hospital, he did a residency at Greenwich Hospital. He eventually received an Army assignment to Puerto Rico, which he followed up with additional training in internal medicine at Johns Hopkins. When he was offered a position on the staff at Greenwich Hospital in 1950, he returned for good to practice internal medicine.

Markley has worn many hats over the years, in addition to founding and directing the home care program. He served as the hospital's electrocardiographer for 24 years; formed the first professional medical corporation in Greenwich in 1963 with three of his fellow internists; served as chief of medical services from 1967 until 1974; and after selling his internal medicine practice in 1979, became medical director of Greenwich Health Examiners, a company that performed

In 2004 Henry Markley retired after a 60-year career in medicine, mostly at Greenwich Hospital in Connecticut. He keeps fit with tennis, golf and a healthy lifestyle.



physicals for executives. In 1993, at 75, an age when most people would have been retired, he cut back his professional activities, limiting himself to running the home care program. Although it wasn't a full-time commitment, he spent a few hours each day at the hospital reviewing charts and coordinating services.

Markley said he continued to work all these years because his father, who lived until the age of 102, retired at 75 and regretted it for the rest of his life. Even though longevity runs in his family, Markley practiced preventive medicine. He is trim, has never smoked, has only an occasional glass of wine and is very active, although age has taken a slight toll. "I'm not any good at tennis any more," he admitted. "I know where I'm supposed to be on the court, but it takes me a while to get there."

Markley married his wife, Nicki, 13 years ago after twice becoming a widower. "The first time I was married for 25 years, the second for 20 years. I told Nicki we're not fooling around this time; we're going for 30 years," he said. Meanwhile, he has other milestones to look forward to. I went to my 60th medical school reunion," he said. "I'm looking forward to the 65th."

—Jill Max

A Montana doctor's 30 years of medicine without a safety net

On January 7, 1984, **Ron Losee**, M.D. '44, tramped out the front door of the hospital in Ennis, Mont., and into the snowy fields, intent on walking to his death. Losee, a general practitioner skilled in orthopaedic surgery, had just learned that he was being sued for malpractice by a woman who claimed that his operation on her ankle caused her undue pain during bowling. "If this was my reward by society for all my years of service, then I didn't want to live anymore. I have always tried to be the best damned doctor I could possibly be," said Losee, who since 1949 had devoted himself to his patients—even offering his own bed to patients before Ennis had a hospital. Fortunately for Losee and his loved ones, fresh bobcat tracks in the snow jolted him back to reality.

"I was fine with falling asleep in the snow and dying, but I didn't want my b***s clawed off by a bobcat," Losee said with characteristic frankness and good humor. He retraced his steps and made it home safely, although cold, cramped and tired.

In the dread-filled, six-month stretch that followed, the claim against Losee was deemed baseless; the woman's discomfort was actually caused by an injury she had sustained after Losee's surgery. However, the distaste this event left him with created the medical maverick that he is today. At the time of the lawsuit, Losee had no medical malpractice insurance. Today, at 86 vigorous years of age, Losee boasts the wherewithal and

gumption to give medical consultations, perform tennis elbow operations and practice medicine without malpractice insurance, just as he has done for the past 55 years.

Losee's decision not to carry insurance was born of practicality and the intimate nature of his practice in a rural mountain hamlet 55 miles southwest of Bozeman. He carried an insurance policy until 1975, when the cost jumped from \$8,000 to \$30,000—slightly more than his net income for the year. Losee simply could not abide passing the financial burden on to the cowboys, farmers, miners and waitresses who were already scraping together as much money as they could to pay for his services.

After the single 1984 lawsuit brought against him, Losee quite happily continued practicing medicine without malpractice insurance. But his insurance ire was rekindled by a letter he received in May 2005 from Blue Cross Blue Shield of Montana informing him that—because he does not carry malpractice insurance—he was no longer a recommended provider. The decision has had little effect on Losee, as patients still seek out his medical services. But after 55 years of sound medical practice, Losee finds it ludicrous that he is being "kicked out" of the medical system, especially since he believes that, depending on the circumstances, some doctors who commit malpractice deserve to be imprisoned. He penned a letter to Blue Cross Blue Shield sharing his strong views about the malpractice insurance industry and, as he said, "to teach them some manners." In their response, Blue Cross Blue Shield said requiring

Ron Losee dropped his malpractice insurance 30 years ago when the cost more than doubled, and he felt he could not in good conscience pass the expense along to his patients.



malpractice insurance is an industry standard designed to protect members.

In his letter, Losee detailed what he considers serious flaws in the system. “In Montana, about one-third of malpractice claims progress to lawsuits. Of these, only a small proportion end in jury trials, with physicians prevailing in the bulk of those cases,” wrote Losee, who has served on the nonbinding Montana Medical Legal Panel, which comprises three doctors and three lawyers who evaluate malpractice claims to recommend whether they should proceed to trial. Malpractice insurance is, he believes, rarely needed, but the insurance industry has instilled a sense of fear in both doctors and patients to maintain the system. This fear, Losee asserted, is largely accomplished by a “bribeocracy” system of government: congressmen and senators receive large financial backing from trial lawyers and insurance-industry lobbyists to fund their re-election campaigns, while the elected officials, in return, fuel the malpractice insurance fire.

As an alternative, Losee advocates a no-fault medical liability compensation system. Instead of going to court, a malpractice claim would go to an expert panel that would assess whether an

injury has indeed been caused by a physician or other health care provider. Compensation would be doled out from a pool of money collected from tax revenues or premiums charged to doctors.

Sitting on his porch and looking out over the Madison River to the snow-capped peaks of the Rocky Mountains, Losee often reflects on his many joyful years of practice in Ennis, which began when he, his wife and their 2-year-old daughter trekked to Montana from Connecticut in 1949 in their Army Jeep. Being dropped from Blue Cross Blue Shield’s provider network has certainly not slowed Losee’s practice. Widely acclaimed as a physician who made major headway toward understanding and surgically repairing the “trick knee” (the Losee tests bear his name), he still sees patients and operates on tennis elbows. Patients seek Losee out and return to him time and again, based on his medical expertise and sincerity rather than the amount of malpractice insurance he carries.

—Kara A. Nyberg

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, P.O. Box 7612, New Haven, CT 06519-0612.

The passing of two with years of service to the medical school

As the new year opened, *Yale Medicine* received word of the passing of two people with long-standing connections to the School of Medicine.

Connie Quick Tolliver, who worked for more than 30 years in the Office of Alumni Affairs at the School of Medicine, died in Hamden, Conn., on December 24 of heart failure. She was 66. Tolliver, who retired in 1995, served as assistant to the director of alumni affairs.

Henry Martone Sr. died in Daytona Beach, Fla., of complications of diabetes on December 27. He was 69. Martone was a familiar presence at the annual reunions, driving a van that shuttled alumni among various tours and dinners.



Robert Finkel



Ralph Greco



Noreen Rossi



Rock Positano and Rudolph Giuliani



Anu Gupta and Arnab Ghatak

Mary L. Warner, M.M.Sc., PA-C, assistant dean and director of the Physician Associate (PA) Program, met with PA alumni in Falmouth, Maine, in August. Joining them was Ruth Cole, widow of Jack W. Cole, M.D. '66, former chair of surgery, who founded the PA program in 1970. Attending the gathering were Frank J. Noreika, PA '94; his wife, Stacy; Lauren T. Ormsby-Pieri, PA '85; Cary J. Stratford, PA-C '80; Michelle A. Roy, PA '98; Lisa Brown, PA '04; and Sherrie A. Downing, PA-C '93.

1940s

David E. Morton, M.D. '48, HS '55, writes to say that his third granddaughter, Kan Kojima, was born last year and that he has been working on the biography of his great-grandfather, Edwin Emery. Emery, a hero on the Union side during the Civil War, was an instructor for the Revenue Cutter Service, a forerunner of the Coast Guard.

1950s

Gerard N. Burrow, M.D. '58, HS '66, has been named chair of the board of the University of Connecticut Medical Center and a trustee of the University of Connecticut. Burrow, who is president and CEO of the Mystic Aquarium & Institute for Exploration, is the David Paige Smith Professor Emeritus of Medicine and dean emeritus of the Yale University School of Medicine.

1960s

Robert I. Finkel, M.D. '65, writes to say that he retired on July 1, 2005, after 32 years of practicing

rheumatology at the Toledo Clinic. He plans to devote his energies to other interests, hobbies and, hopefully, travel.

Ralph S. Greco, M.D. '68, HS '73, the Johnson & Johnson Distinguished Professor and chief of general surgery at Stanford University School of Medicine, is one of 10 recipients of the 2006 Parker J. Palmer Courage to Teach Award, given by the Accreditation Council for Graduate Medical Education.

Karen H. Toker, M.D. '67, received the first Francis Edwards Rushton Award last year from the University of Florida Department of Pediatrics for her work in community pediatrics and child advocacy.

1970s

Robert H. Posteraro, M.D. '73, HS '78, FW '79, a radiologist with Lubbock Diagnostic Radiology in Lubbock, Texas, graduated from Oregon Health and Science University with the degree of Master of Biomedical Informatics last June.

Noreen F. Rossi, M.D. '78, professor of medicine and physiology at Wayne State University School of Medicine, has been awarded a \$1.6 million, five-year grant from the National Heart, Lung, and Blood Institute of the National Institutes of Health. She will study how regular exercise decreases blood pressure.

Alvin H. Strelnick, M.D. '75, chief of the Division of Community Health in the Department of Family and Social Medicine at Montefiore Medical Center, received the 2005 Honorary

Alumnus Award in June from the Albert Einstein College of Medicine of Yeshiva University in New York. In October he received the "Family Medicine: The Power to Change Our World" award at the northeast regional meeting of the Society of Teachers of Family Medicine.

1980s

Troyen A. Brennan, M.D. '84, J.D. '84, M.P.H. '84, professor of medicine at Harvard Medical School and professor of law and public health at the Harvard School of Public Health, has been elected to the Institute of Medicine. His research group focuses on the interwoven issues of improving patient safety and addressing the crisis in medical malpractice.

Rock G. Positano, D.P.M., M.Sc., M.P.H. '89, received a Spirit of Cabrini Award at the Cabrini Mission Foundation 2005 Gala and Awards in New York City on November 3. Also honored were NBC "Today" co-host Katie Couric and former mayor Rudolph W. Giuliani, and his wife, Judith S. Giuliani.

Positano, co-director of The Foot Center at the Hospital for Special Surgery in New York, delivered the keynote address.

1990s

Lee M. Akst, M.D. '99, was married in October to Jodi S. Wilkoff in Cleveland. Akst, who graduated from Yale College in 1995, is a fellow in laryngology at Massachusetts General Hospital. His wife is a partner in The New Teacher Project, an educational consultancy in New York.

Pauline W. Chen, M.D., HS '98, has won the Staige D. Blackford Prize for Nonfiction from the *Virginia Quarterly Review*, for her article, "Dead Enough?: The Paradox of Brain Death," published last fall.

Anu Gupta, M.D. '97, HS '00, FW '02, was married in November to Arnab Ghatak, M.D., M.B.A., in Roslyn, N.Y. Gupta directs philanthropic programs for HIV/AIDS and women's and children's health at Johnson & Johnson in New Jersey. Ghatak consults on pharmaceuticals and medical devices for McKinsey & Co.

Tim Mello, PA '99, and **Alice (Hofmann) Mello**, PA '99, announce the birth of their second child, Margaret Ella. Tim practices at Connecticut Valley Orthopedics and Sports Medicine in Springfield, Vt., and Alice practices in pediatric neurology at Dartmouth-Hitchcock Medical Center in Lebanon, N.H.

Gualberto Ruano, Ph.D. '92, M.D. '97, president and CEO of the biomedical company Genomas, received the BEACON Medical Technology Award in September in recognition of his contributions to personalized medicine. BEACON (Biomedical Engineering Alliance and Consortium) is the professional association of the medical device industry in Connecticut.

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Remi J. Cadoret, M.D. '53, died of prostate cancer at his home in Iowa City, Iowa, on November 12. He was 77. After graduating from the School of Medicine, Cadoret spent two years in the U.S. Air Force, during which time he delivered 500 babies. He did research at the Duke University Parapsychology Laboratory in North Carolina before taking a position at the University of Manitoba College of Medicine in Canada. From there he went to Washington University in St. Louis and the University of Iowa. He was director of the Iowa Consortium for Substance Abuse and Evaluation. After his retirement in 1998 he continued his research, using adoptee studies to study gene-environment interaction, with a focus on antisocial behavior and substance dependence.

Ludmil A. Chotkowski, M.D. '42, of Berlin, Conn., died on October 6 at the age of 89. Chotkowski was an internist for more than 50 years at New Britain General Hospital, the Rocky Hill (Conn.) Veterans Home and Hospital and Connecticut Valley Hospital. He was also a self-published author, columnist, community activist, naturalist and farmer with a 14-acre fruit orchard. In Berlin, where he was born and raised on a family farm, he served as health officer, improving water quality and introducing innovative public health measures. He established one of the first clinics to administer polio vaccinations, and he performed kidney dialysis and recommended inhalers to treat asthma before these practices were widely used. In another way, however, he remained old-fashioned, continuing to make house calls.

Michael T. Cronin, D.V.M., Ph.D., M.D., HS '67, assistant clinical professor of pathology, died in Branford, Conn., on November 23 of Parkinson's disease. He was 81. Cronin's medical career spanned 30 years at Yale, the Hospital of Saint Raphael and Memorial Hospital in Meriden, Conn. Early in his career, Cronin, a native of Ireland, did veterinary research at the Irish Racing Board and the Equine Research Station in England. From 1971 to 1989 he was a consulting editor for the magazine *American Scientist*.

Armin F. Funke, M.P.H. '60, died on June 24 in Roseville, Calif. He was 78. Born in Germany, Funke came to the United States in 1948 and worked at the state of California Department of Health for 30 years.

Joshua C. Gibson, M.D. '01, died on November 14 in New York of a cardiac arrhythmia. He was 34. Gibson was a fellow in infectious diseases at the Mount Sinai School of Medicine, where he co-founded the Advancing Idealism in Medicine Curriculum to help residents get involved in international programs that focus on improving the plight of others. Gibson himself worked at a refugee camp in Tanzania for Rwandan refugees, volunteered at a rural health center in India and tracked the health impact of the World Trade Center attacks on rescue workers. At a memorial service, Daniel S. Caplivski, M.D. '00, an assistant professor at Mt. Sinai, recalled his classmate, friend and colleague: "We had seen each other as first-year medical students just learning to listen through a stethoscope. Now I was watch-

ing his wonderful bedside manner and I saw his deep compassion and his meticulous attention to detail. He had become a great doctor."

James H. Greenwald, M.D. '58, died on November 14 in Chicago. He was 73. Greenwald served his internship and residency at Cook County Hospital in Chicago, then practiced nephrology and internal medicine in the Chicago area until he retired in 2000. He was a member of national medical societies and the author of several research papers.

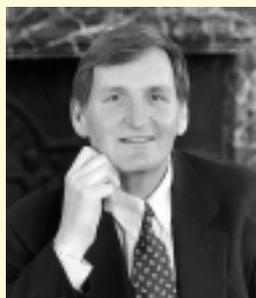
Martha F. Leonard, M.D., a former professor of pediatrics long affiliated with the Child Study Center, died on December 27 in North Branford, Conn. She was 89. Leonard came to Yale in 1961. As an early-childhood specialist, she provided compassionate care to children and their families. She also worked to influence legislation affecting children. She was active in the Center Church in New Haven, the Interfaith Cooperative Ministries and the Community Foundation for Greater New Haven. In 1979 she received an honorary M.A.H. degree from the Yale Divinity School and later served as chaplain at the Evergreen Woods retirement community in North Branford, where she lived.

Mary Ann Lillie, R.N., M.P.H. '87, died on October 4 at the Connecticut Hospice in Branford, Conn. She was 54. Lillie worked for many years at Yale-New Haven Hospital and was an active member of St. Andrews United Methodist Church in New Haven.

Patrick J. McLaughlin Jr., M.D. '48, died on September 8 in Massachusetts at the age of 82. McLaughlin was a social worker for the city of Lowell and the Commonwealth of Massachusetts. For many years McLaughlin, who started but did not complete his medical education at Yale, and his wife lived in Andover, Mass., but recently moved to Concord to be near one of their daughters and her family.

Kay Tanaka, M.D., D.Sc., professor emeritus in the Department of Genetics, died on August 21 in New Haven. He was 76. Before coming to Yale in 1973, Tanaka held faculty positions at Baylor College of Medicine, Harvard Medical School and Massachusetts General Hospital. He founded and, from 1977 to 1989, directed the Biochemical Disease Detection Laboratory at Yale, and in 1987 he received a MERIT award from the National Institutes of Health. He was a pioneer in the use of gas-liquid chromatography and nuclear magnetic resonance in the identification of inherited metabolic diseases.

Wilbur D. Van Buren, M.D., Ph.D., died on November 6 in Kansas City, Mo., of pancreatic cancer. He was 57. Van Buren began his medical studies at Yale, but obtained his degree at St. Louis University. Known as "the singing doctor," he was in private practice and worked at hospitals and nursing homes in Kansas City. He was a major in the U.S. Army Reserves, a Grand Knight of the Knights of Columbus and active in the Holy Name Catholic Church.



MICHAEL MARSLAND

A new center to fight obesity

A decade ago, when Kelly D. Brownell, PH.D., first started attracting national attention, his critics called him a “wacko,” a “food fascist” and the “grand poobah of the anti-consumer movement.” His crime? Accusing the food industry of creating a “toxic food environment” resulting in an “obesity epidemic” (See “Fighting the Good Food Fight,” Winter 2004). Three years ago he outlined the problem and proposed solutions in *Food Fight*, written with Katherine Battle Horgen, PH.D.

His goal since then has been to “change the world’s diet,” he said. “It took a long time to take the first few steps, but now things are starting to happen quickly.”

One of those advances is Yale’s new Rudd Center for Food Policy & Obesity, which Brownell, professor and chair of psychiatry and professor of epidemiology, directs. Made possible by a gift from Leslie Rudd, a vintner who hopes to affect attitudes toward food and wine in this country, the center’s goal is to improve the world’s nutrition, prevent obesity and reduce weight stigma through science-based public policy. The center opened its new offices on Edwards Street in October.

“We need to do strategic science in the interest of informing policy leaders,” said Brownell, “and we also want to make policy-makers more responsive to science.” As an example, Brownell cited the debate over soda machines in schools. “While educators may know that soft drinks aren’t especially healthy, health isn’t the main reason schools are in business. But if we can show that diet affects standardized test scores, you’d see an immediate application for public policy. That’s strategic science.”

The center’s work will involve both domestic and global initiatives, said Brownell, a reflection that the obesity crisis is worldwide. “The health minister of China recently announced that obesity and diabetes were huge problems there. The same is true in India,” he said. “You can’t understand the modern food environment without a global view. National trade policies, subsidies to the agricultural industry—all these things affect the food supply worldwide.” In addition, much obesity-related policy innovation—taxing junk food, for example—is occurring outside the United States.

“We really do want to make a difference,” said Brownell, who was named to the Institute of Medicine in October.

—Jennifer Kaylin



MAY 1956
Alumni Bulletin

The Dean’s Report

“In his annual report to the alumni of the School of Medicine on February 22, Dean Lippard reviewed the progress of the school over the past thirty-five years and outlined plans for its future development.

“Under the guidance of Drs. Blumer and Winternitz and with renewed interest of the university, the school underwent a major transformation shortly after the First World War. The faculty was reorganized, new buildings were erected, financial support was improved and enrollment increased. Graduating classes, which averaged 13 in the decade 1910-20, have increased to 80. ...

“This program [the Yale System] also requires a superior faculty, including a substantial nucleus of men who are dedicated to full-time teaching, research, and care of patients within a university hospital. ...

“The school has been successful over the years in attracting such men, and the full-time faculty now numbers about 200. Efforts have been made in recent years to strengthen clinical fields such as psychiatry, dermatology, hematology, neurology, and cardiovascular surgery, not previously represented on the full-time staff, and to broaden the range of special interests in the basic science departments. ...

“Improvement in facilities has kept pace with other developments. Most of the Medical Center has been built since 1920. The most impressive additions in the last five years are the Edward S. Harkness Memorial Hall, the Memorial Unit of the Grace-New Haven Community Hospital, and an extension of the Lauder Building for animal quarters.”



WINTER/SPRING 1981
Yale Medicine

“From This Small Sapling ...

“On December 1, shortly after noon, five men from the School of Medicine gathered in the courtyard outside the Medical Library. Some had shovels. They had come to plant a rare Oriental plane tree sapling, alleged to be a descendant of the ‘Tree of Hippocrates,’ under which the 5th-century Greek physician taught the art and science of medicine.

“The sapling was grown from seeds presented to Dr. Silver for the School of Medicine by Dr. William C. Gibson, chairman of the Universities Council of British Columbia, and a former student of Dr. John F. Fulton, the first chairman of the Department of the Hospitals of Medicine at Yale. Dr. Shope took 25 of them to his brother, William Flemer III (M.A. ’47) of the Princeton Nurseries, Kingston, N.J., who planted and nurtured them.

Seven of the rare seeds germinated. If the one planted in the library courtyard survives the winter, the others will be planted nearby. Admittedly, the sapling is scarcely more than a twig, but historians typically are optimists. “The purpose of this endeavor is to establish a small park—a ‘Hippocratic Grove,’ with benches and a patio,” said Dr. Viseltear. “It would be a place for contemplation and study, or a pleasant spot to enjoy one’s lunch and pass the time of day.”

NEW BUILDINGS REFLECT COMMITMENT TO SCIENCES

The dedication of two new buildings on the main campus in October highlighted the university's commitment to scientific research and education. The Department of Biomedical Engineering got a new home in the Daniel L. Malone Engineering Center, a five-story, 63,117-square-foot building on Prospect Street. Research there will focus on biomedical engineering, materials science and nanotechnology. The construction was made possible by a \$24 million gift from John C. Malone, a 1963 Yale College alumnus and chair of the Liberty Media Corp., and is named for his father, an engineer at General Electric.

"It stands as a statement to all that Yale engineering is an integral part of this university's most vibrant intellectual life," said Paul A. Fleury, PH.D., dean of the Faculty of Engineering. "The research and teaching that will take place here will center upon those forefront areas of biomedical engineering, materials science and nanotechnology that underpin 21st-century progress."

Also on Prospect Street is the 105,000-square-foot, three-story Class of 1954 Chemistry Research Building, the result of the largest class gift in the university's history. Each floor is dedicated to one of three areas: synthetic organic chemistry, inorganic chemistry and chemical biology. Projects under way include developing new materials for solar energy and new catalysts to facilitate hydrogen storage as a fuel source, and investigating the molecular basis for energy transduction in plant photosynthesis.

Provost Andrew D. Hamilton, PH.D., said a collaboration among the administration, the faculty and the Class of 1954 made the building possible. At the dedication Hamilton had a representative of each group help create a chemical reaction in which three clear liquids were mixed together before the solution turned to Yale blue. "It only works when all three components of the reaction are present," Hamilton said. "Cooperation is vital for continued Yale success, as this reaction continues again and again and again."

—John Curtis



MICHAEL MARSLAND

The Daniel L. Malone Engineering Center is one of two new buildings on Yale's central campus that is devoted to science.

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