

Yale Medicine

summer 2003

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A new space for science



With the opening of The Anlyan Center for Medical Research and Education, the school dedicates its largest building ever.

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SUMMER 2003

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info.med.yale.edu/yymm

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 Anlyan Center for Medical Research and Education devotes more than 450,000 square feet of new space to the study of science and the training of new generations of scientists and physicians.

Photographs by Frank Poole (6) and Martin Klimek (portrait).

THIS PAGE

The new building at 300 Cedar Street is now the largest facility at the medical school, dominating the skyline at the corner of Cedar Street and Congress Avenue.

Photograph by Frank Poole

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Avoiding medical errors is one piece of the malpractice puzzle. David Gaba has spent his entire career preventing them.

By Paul Chutkow



Above and beyond the call at Commencement

On behalf of my family and myself, I want to express my gratitude to the entire staff who organized, reorganized and ran the Commencement ceremonies. Though I wasn't there beforehand to witness the Herculean effort, my father was—and he reported that everyone worked like Trojans to preserve the celebration of the day. I don't think I'm capable of expressing how important that was to my family, and how it left them with a sense that this school—the entire school—has an unusual and strong sense of community. I'm proud to have been a part of it, and overjoyed to remain one.

The most exciting, emotional and meaningful moment of the day occurred as I and my classmates took our short walk from the I-wing of Sterling Hall of Medicine into the graduation tent. We were a little depressed as we stood dripping onto the floor of Sterling. Someone near me mentioned that we looked like a funeral procession as we shuffled silently toward the exit. As we neared the door I saw staff members standing side by side, holding umbrellas for us. I was overwhelmed by the abrupt contrast between my momentary depression and the emotions that resulted from the cheers emanating from the tent and the stage. The applause didn't even threaten to lull, let alone pause or stop.

To the staff who made it all happen, I thank you for everything you did for our class to make the best of a difficult day. And I thank you, in particular, for helping my own family. We appreciate it deeply.

Maxwell S. Laurans, M.D. '03
New Haven

As we went to press, the kudos were flying

Each spring the National Academy of Sciences elects new members, bestowing one of the highest honors a U.S. scientist or engineer can receive. As this issue of the magazine was in production, we learned that three Yale scientists had been tapped for membership: medical school faculty members Linda M. Bartoshuk, Ph.D., and Arthur L. Horwich, M.D., HS '78, FW '84, and alumnus John D. Baxter, M.D. '66, HS '68, professor of medicine at the University of California, San Francisco (UCSF).

Bartoshuk, a professor of surgery (otolaryngology) and psychology, is an experimental psychologist and one of the world's leading experts on the science of taste. Horwich, professor of genetics and pediatrics and a Howard Hughes Medical Institute investigator, has solved key problems in the study of protein folding, work that has clear implications for Alzheimer's disease.

Baxter is director of UCSF's Metabolic Research Unit. In 1979, he and Howard M. Goodman, Ph.D., were the first to clone the gene for human growth hormone, which became the second genetically engineered product to receive government approval. His current work focuses on how receptors in the nucleus of a cell affect human health and disease.

On another front, judges in the CASE Circle of Excellence competition have selected *Yale Medicine* to receive the silver medal in the Special Interest Magazines category at the CASE International Assembly in July in Washington. *Yale Medicine* was awarded a silver medal last year as well by CASE, the 23,500-member Council for Advancement and Support of Education, and received the highest honor in the 2001 magazine competition sponsored by the Association of American Medical Colleges.

—The Editors

Yale Medicine

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

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This just in

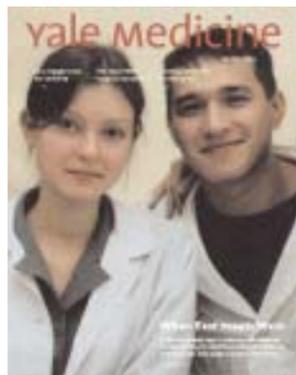
One of the dubious pleasures of editing a magazine is taking an issue that is ready to go to print and remaking it because news has broken. The pleasure is doubtful because once an article, a headline or a layout is complete in the eyes of the person who created it, there is an almost irresistible force that seems to say, "Don't change a thing."

But change was the *modus operandi* at the School of Medicine during May and June this year. The largest building ever constructed on the medical campus was dedicated in May, and news followed soon after that benefactors A. John Anlyan, B.S. '42, M.D. '45, and Betty Jane Anlyan had increased their gift to Yale so significantly that the entire 457,000-square-foot complex would be named in their honor. What had been a two-page follow-up to our Winter 2003 article, "The Big Move," became this issue's cover story ("A New Space for Science," p. 14). We added four pages to the issue to accommodate more photos and to show the progression of the building's construction over the past three years.

Then on June 23 came another news flash, that Dean David A. Kessler, M.D., had accepted an offer from the University of California, San Francisco, to become vice chancellor for medical affairs and dean of the UCSF School of Medicine. Appointed in 1997, Kessler presided over the medical school during a period of major change, an era capped by the opening of The Anlyan Center. Even bigger challenges await him in San Francisco, where UCSF has begun building a phased, 43-acre life sciences campus in the city's Mission Bay district. We wish him well.

Yale President Richard C. Levin has appointed Dennis D. Spencer, M.D., HS '76, as interim dean effective July 1 pending a search for a permanent successor. Spencer, who figures prominently in one of this issue's feature stories ("High Resolution," p. 20) and was profiled in the Fall 1998 issue of *Yale Medicine*, is the chair and Harvey and Kate Cushing Professor of Neurosurgery. We'll follow up on this story with an interview with the new interim dean in our Autumn issue. Meanwhile, rest assured that even during the hazy, lazy days of summer, there is never a dull moment on Cedar Street.

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HOW TO REACH US

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

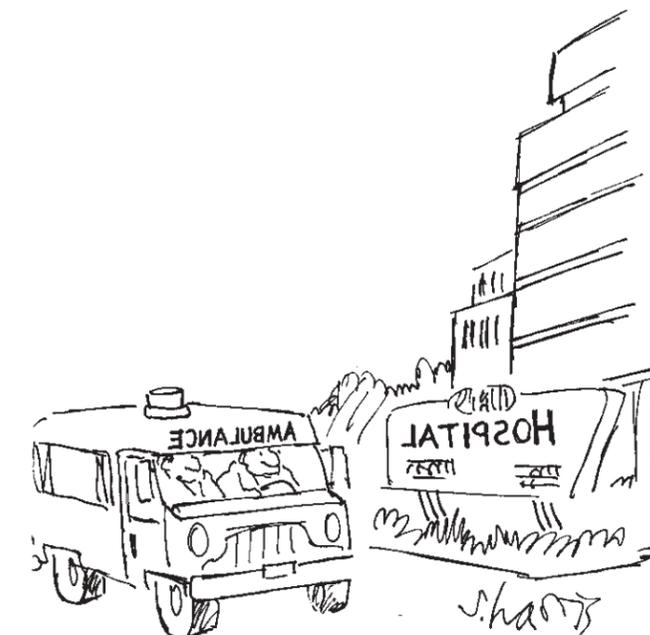
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Dennis Spencer has been named the interim dean of the School of Medicine.

SECOND OPINION BY SIDNEY HARRIS



A new site for sore eyes

After 10 years, doctors and patients welcome the return of an eye clinic to the Hill Health Center.

When Candace Ford went for her exam at the new eye clinic in the Hill Health Center, doctors said they couldn't test her while she was wearing her contact lenses; they wanted to see her glasses. So Ford ran home to get what she needed and was back in the examining chair within minutes.

This kind of convenience for Hill neighborhood residents, many of whom don't own cars, is one of the many reasons health center administrators and doctors in the Department of Ophthalmology and Visual Science wanted to open an eye center in the neighborhood.

The health center used to offer ophthalmology services, but about 10 years ago the program died, forcing many

Hill residents to travel to the medical school for their eye care. "We had a tremendous number of no-shows from the Hill, so we realized the distance patients had to travel was a barrier to access," said Susan H. Forster, M.D., HS '81, an assistant professor in the department. She and others decided the solution was to locate an eye clinic in the same place where patients go for the rest of their medical care.

Organizers applied for and received a \$50,000 grant from the Community Foundation for Greater New Haven, which enabled them to set up the clinic and outfit it with state-of-the-art equipment. Hill Health Center Chief Operating Officer Gary Spinner says the eye clinic is a much-needed addition to the center. "We serve a large population with diabetes who need ongoing eye care to detect and treat the complications that can affect their eyes," he said.

Four chief residents take turns staffing the clinic, which is open one

day a week. Patients are billed for their treatment, but there is a sliding-fee scale for those who don't have medical insurance. "We all felt it would benefit a medically underserved population as well as the medical residents who rotate through here," Spinner said. "They learn a lot about providing health care beyond the technical end of it."

Although the clinic has been open only since January, Forster said it already served about 20 patients a day and was booked through June. The clinic provides vision tests and screening for such conditions as glaucoma, amblyopia (lazy eye) and retinopathy, which is linked to diabetes. Patients who need surgery or a diagnostic procedure are referred to Yale. Forster said the clinic's close ties with the ophthalmology department allow patients to benefit from the expertise of Yale specialists, who have ongoing consultations about patient care with the on-site residents.

Guy Jirawuthiworavong, a third-year ophthalmology resident, examined the eyes of Michael Stallings at the Hill Health Center on a Wednesday in April. A grant from the Community Foundation for Greater New Haven has allowed the center and the medical school to bring eye care to the neighborhood.



TERRY DAGRADI

Contract still unresolved, union strikers spend five days out in the cold

During a week of subfreezing temperatures, a heavy rain and a blizzard, thousands of Yale employees, including hundreds at the medical school, took to the streets in March to strike over contract negotiations that had stalled over wages, job security and pension benefits. The strike had clerical and technical workers from Local 34 and service and maintenance employees from Local 35 sharing picket lines with hundreds of graduate students from GESO, the Graduate Employees & Students Organization, which is seeking union recognition from the university. The unions also support the right of hospital workers to unionize.

Over the course of the weeklong strike, the unions held rallies at Woolsey Hall, Phelps Gate and the medical school, led by supporters including the Rev. Jesse Jackson, New Haven Mayor John DeStefano Jr., U.S. Rep. Rosa DeLauro, local clergy and local and national union leaders. Disruptions at the medical school appeared to be minimal—58 percent of Local 34 workers remained on the job.

Each side blamed the other for the impasse. Union leaders said the university had refused to budge on its offers. The university accused the unions of linking contract negotiations with GESO's organizing efforts and with a drive by the Service Employees International Union to organize service and other nonprofessional employees at Yale-New Haven Hospital. The university opposes unionization of graduate students and says the hospital is a separate entity from the university and that workers there must decide whether to unionize.

In April Local 34 rejected the university's 10-year contract proposal, and in early May graduate students rejected GESO as their bargaining agent.

—John Curtis

While convenience was a major selling point for Ford when she decided to go to the eye center, she also appreciated the quiet, relaxed atmosphere. "They had the radio playing R&B, it was clean and there was only one person ahead of me," she said, "so I was in and out real quick."

Guy Jirawuthiworavong, M.D., a third-year ophthalmology resident who works in the clinic, also enjoys the intimate atmosphere. "It's been a really great experience," he said. "Community clinics by nature are smaller and homier. I like the family setting."

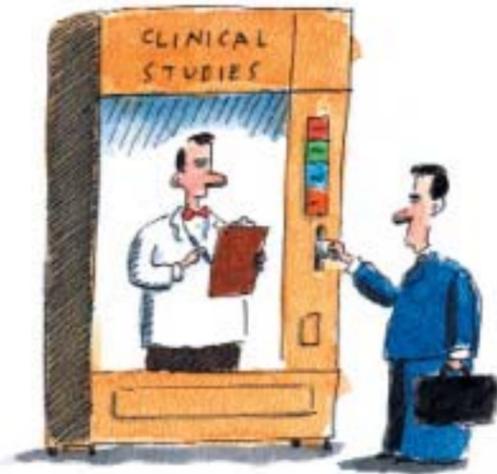
He said the majority of his patients have a family history of glaucoma and want to get their eyes checked, or they need an annual screening for diabetes. This is just the news Forster wanted to hear. She said many people overlook preventive eye care until it's too late. "Our goal with this center is to catch things early."

—Jennifer Kaylin



JOHN CURTIS

Graduate students at the medical school picketed outside the Sterling Hall of Medicine during a weeklong strike in March by workers from Locals 34 and 35. In a vote in April graduate students rejected a bid by GESO to represent them.



GARY CLEMENT

Does industry funding equal conflict of interest? Often it does, Yale authors claim

As biomedical researchers increase their dependence on industry support for research, Yale investigators say this relationship has led to “pervasive and problematic” conflicts of interest. Between 1980 and 2000, while the federal government’s share of funding fell, industry support rose from 32 percent to 62 percent.

The Yale team found that business-sponsored studies are far likelier to yield results favorable to the industry than those funded by sources without a vested interest, such as the federal government. They also found that industry studies are designed to favor such results, that negative outcomes meet with delays in publication or aren’t published and that many researchers and institutions have financial ties to their sponsors.

“Industry sponsorship has the potential to distort the scientific process in a very disturbing way,” said Cary P. Gross, M.D., an assistant professor of medicine and the study’s lead author. “I am in no way against industry sponsorship,” he said, noting that he has taken part in such studies. “But our results show that we need very close oversight.”

The team’s review of 37 studies on the extent and impact of conflicts of interest appeared in January in *JAMA: The Journal of the American Medical Association*. They found that studies sponsored by industry were 3.6 times more likely to have conclusions favorable to industry than studies without that support.

Industry studies also tended to compare an industry’s drug to a placebo instead of a drug already on the market, said Justin E. Bekelman, a fourth-year medical student and a study co-author. “Placebo-controlled trials are likelier to end with positive results,” he explained. Another study found that when the industry’s drug was compared to a medicine already on the market, patients were given inappropriate doses of each drug in a way that supported the newcomer.

When results didn’t favor the industry-sponsored therapy, publication was delayed or reports were not published at all. Sometimes studies were stonewalled while the industry sought patents; at other times, some researchers were denied access to the data.

“It’s very important that all trial results, whether positive or negative, be published,” said Bekelman.

The study also found that a quarter of investigators have industry affiliations, and that two-thirds of academic institutions (including Yale) hold equity in startup firms founded upon research at those institutions. Gross said that universities must erect a “very firm fire wall” to avoid conflicts of interest.

Bekelman said a “balance of power” is needed. Academia and medical journals have begun to insist on more financial disclosure and access to data. But more needs to be done, Bekelman said, because without complete and unambiguous disclosure, the research “will not serve the needs of patients or our health system well over the long term.”

—John Dillon



MICHELE FLAGGE

A WINNING SPIRIT

When 12-year-old Millie Suggs rode her wheelchair in a Family Fun race at Disney World in January, two second-year medical students offered moral and medical support. Deborah Kaplan, who met Millie six years ago through her sister, a teacher, ran in a marathon while Michele Flagge accompanied Suggs during the 5-kilometer race. Suggs, who suffered a spinal cord injury in a car accident when she was 2, won a prize as the only wheelchair racer. Thanks to her friendship with Suggs, Kaplan wants to be a pediatric physiatrist when she graduates. “Millie has taught me so much about the human spirit,” she said.

—Jennifer Kaylin

NIH awards Yale \$18 million to develop new technologies for proteomics research

The university has received an \$18.2 million award from the National Institutes of Health to establish one of 10 national centers to develop proteomic technologies for the diagnosis, understanding and improved treatment of heart, lung and blood disorders.

The National Heart, Lung and Blood Institute (NHLBI) Proteomics Center will bring together 21 Yale faculty from 12 departments and will build on the expertise of the Howard Hughes Medical Institute (HHMI) Biopolymer/Keck Laboratory at Yale University, one of the largest biotechnology laboratories of its kind in academia. The Proteomics Center is headed by Kenneth R. Williams, Ph.D., director of the HHMI/Keck Laboratory and professor (adjunct) of research in molecular biophysics and biochemistry. The center will focus on two technologies: proteome profiling

and synthetic peptide-based reagents to block specific protein-protein interactions. The latter effort will be directed by the co-investigator on the NHLBI contract that established the center, William C. Sessa, Ph.D., director of the Yale Vascular Cell Signaling and Therapeutics Program and professor of pharmacology.

“By developing two complementary technologies in parallel, we hope to use protein profiling to identify key proteins involved in diseases of the heart, lung and blood and then develop novel reagents capable of specifically blocking the activities of those proteins,” Williams said. “The overall goal is to increase our understanding of the disease process, which should lead to more effective treatment.” Additional information and continuing updates on progress of research carried out in the Yale/NHLBI Proteomics Center may be found at <http://info.med.yale.edu/nhlbi-proteomics/>.

—John Curtis

et cetera ...

THE THESIS GOES DIGITAL

With a vision of electrons prevailing over paper, Charles J. Greenberg, M.L.S., M.Ed., head of reference services at the Cushing/Whitney Medical Library, has launched the Yale Medicine Thesis Digital Library (YMTDL), an online collection of the theses required of all Yale medical students.

The YMTDL debuted in February at <http://ymtdl.med.yale.edu>. The Internet, Greenberg said, has become the “number-one way” of accessing medical research, as foot traffic falls at the library.

Greenberg’s biggest challenge has been to convince students that publishing online won’t harm their chances of publication later in a scholarly journal. Students may delay online publication for up to three years, but abstracts are automatically included on the website.

Last year 12 students agreed to provide their theses; this year Greenberg hopes to get 40. Eventually, he expects that all theses will be available online.

—John Dillon

TWO YALE EXPERTS ON BIOETHICS PANEL

As medical and ethical concerns move from the laboratory to the front page, the Bush Administration has named 11 people, including two experts with ties to Yale, to serve on a new advisory committee on federal protections for human research subjects. The panel is charged with reviewing regulations aimed at safeguarding volunteers in medical and behavioral studies.

“There’s more of a consumer interest and input into bioethics than in the past,” said Celia B. Fisher, Ph.D., director of the Center for Ethics Education at Fordham University and a visiting bioethicist in residence at Yale. Fisher is especially interested in examining protections for special populations, such as pregnant women, prisoners and children. How federal guidelines should be applied to embryos is expected to be one of the more controversial issues the panel considers.

Mary Lake Polan, Ph.D. ’70, M.D. ’75, HS ’77, chair of the Department of Gynecology and Obstetrics at Stanford University School of Medicine, was also named to serve on the panel.

—Jennifer Kaylin



“Hidden” fat poses serious health risk

But exercise can take off invisible pounds and reduce risks of cancer, heart disease and diabetes.

Postmenopausal women who exercise regularly won't necessarily see dramatic changes on their bathroom scales or in their dress sizes, but according to a new study the workouts can have a significant beneficial impact.

They can “exorcise” invisible intra-abdominal body fat that wraps itself around internal organs and may pose a greater health risk than more obvious “love handles” or bulging bellies. It is dangerous, researchers say, partly because it's invisible.

“When you look in the mirror, you don't know how much you have,” said Melinda L. Irwin, M.P.H., Ph.D., assistant professor of epidemiology at the School of Public Health and lead author of the study published in the January 15 issue of *JAMA: The Journal of the American Medical Association*.

Women, who gain an average of a pound per year, tend to accumulate it after menopause, and men are also susceptible to health risks as they gain weight around their middles. Although thin women can have intra-abdominal fat, those with waist circumferences of more than 35 inches are the most likely candidates. According to Irwin this hidden fat has been linked to insulin resistance, type 2 diabetes, hypertension, cardiovascular disease and high cholesterol levels, and increases the risk of breast and colon cancers. Intra-abdominal body

fat is a metabolically active fat tissue because of its shared circulation with the organs it surrounds.

The study, conducted by Irwin and colleagues at the Fred Hutchinson Cancer Research Center in Seattle, Wash., looked at 173 physically inactive postmenopausal women between the ages of 50 and 75. The women were assigned to one of two groups; one exercised at a moderate intensity five days a week and the other merely stretched one day a week. The researchers measured changes in weight and body fat at the start of the study and after one year.

“While overall weight loss was modest for the women who exercised, intra-abdominal body fat loss was statistically and clinically significant,” said Irwin. The study found that women who exercised moderately five times a week saw a 6 to 11 percent decrease in intra-abdominal body fat. “That would translate into a reduced risk of cardiovascular disease and cancer,” Irwin said. “The good news,” she said, “is that even if exercise doesn't seem to be making any visible difference—women only lost, on average, three pounds—moderate exercise such as brisk walking reduced hidden fat.”

According to Irwin, most studies that examine the correlation between weight and exercise just weigh the test subjects and measure their waist circumferences. This merely measures weight, not total body fat or fat distribution. “Usually they conclude that exercise has minimal or no effect on body weight,” Irwin said. “We agree with them, except they're not taking into consideration

body fat and how it is distributed on the body.”

Irwin said she and her colleagues used computed tomography—“which is a lot more sensitive than just getting on a scale and measuring weight”—to gauge the test subjects' amount of intra-abdominal tissue. Using this method, the researchers were able to observe a statistically significant effect of exercise on the intra-abdominal tissue.

The message to take away from this study, Irwin said, is that if you are

getting frustrated because you are exercising but not losing any weight, keep at it. “Even if you think you aren't getting any benefit, you really are.” She also noted that when weight is lost through exercise, rather than diet, you have a better chance of keeping it off. “Dieting hasn't been shown to be good for weight maintenance; you gain it back, whereas if someone exercises to lose weight, they're more likely to maintain the weight loss,” Irwin said.

—Jennifer Kaylin

OVARIAN TUMORS NEED NOT CAUSE INFERTILITY

A conservative approach to the treatment of a rare form of ovarian cancer, called ovarian germ cell malignancies, allows young women to conceive afterwards, Yale scientists have found. In a study published in the February issue of *Obstetrics & Gynecology*, Peter E. Schwartz, M.D., HS '70, the John Slade Ely Professor of Obstetrics and Gynecology, followed the cases of 86 women, most of whom had undergone fertility-preserving treatment in which only the affected ovary was removed. Of 38 women who attempted to conceive, 29 became pregnant. To date, their children have shown no developmental abnormalities.

—John Curtis



et cetera ...

SEIZURES AND DRUG RESISTANCE

Researchers have shown for the first time how long it takes to establish resistance to drugs that control partial epilepsy. A multi-center study directed by Susan S. Spencer, M.D., FW '78, professor of neurology, and published in the journal *Neurology* in February examined 333 patients to analyze outcomes of surgical treatment of partial epilepsy and to identify factors that predict when seizures become intractable. About 80 percent of those with partial epilepsy cannot control seizures with medications.

Researchers found that an average of about nine years passed before at least two drugs failed to control recurrent seizures. During that interval, a quarter of those in the study had remissions lasting up to a year and slightly fewer than 9 percent had remissions of five years or more. A younger age at the onset of seizures predicted longer seizure-free intervals. “This kind of information,” Spencer said, “leads us to explore the mechanisms by which treatment resistance develops over so many years, and prompts consideration and investigation of preventive strategies for the future.”

—John Curtis

A NEW CARDIAC RISK FACTOR

Women with a history of pre-eclampsia are at increased risk for cardiovascular disease, according to a study presented in February at the Society for Maternal-Fetal Medicine annual meeting in San Francisco.

“Pre-eclampsia should be added to the list of risk factors for cardiovascular disease, possibly equal to issues such as obesity, smoking and diabetes,” said Edmund F. Funai, M.D., assistant professor of obstetrics and gynecology and the study's lead author.

Pre-eclampsia, a progressive disease that occurs late in pregnancy and affects about 5 percent of women, can cause slower-than-normal fetal growth and put women at risk of lung, kidney and liver problems. High blood pressure is an early warning sign of pre-eclampsia. The study by researchers at Yale and in Israel tracked the death rates of 34,000 women who gave birth between 1964 and 1976.

—John Curtis

A link between sugar and heart defects

Examining role of glucose in cardiac malformation, researchers look for ways to protect the infant heart.

It's a heart-rending legacy: mothers who have uncontrolled diabetes during pregnancy are three times more likely to give birth to babies with malformed hearts than are mothers whose blood sugar levels are normal. Doctors have known that for some time, but recent work by researchers at Yale and the University of Arizona helps explain how high blood glucose levels in the mother lead to infant heart defects, and may suggest ways to prevent the problem.

"Lack of control of glucose in early pregnancy is a serious problem, because often the woman doesn't even know

she's pregnant at the time," said Joseph A. Madri, PH.D., M.D., HS '76, FW '80, professor of pathology and co-director of medical studies. "Yet this period of the first few weeks is critical, because this is when formation of all the organs occurs."

In earlier work, Madri and co-workers including Emese Pinter, M.D., an associate research scientist in pediatrics, studied the formation of blood vessels of the yolk sac in a mouse model of maternal diabetes. "We found that higher levels of glucose, comparable to what would be found in a diabetic mother, had profound effects on the development of yolk sac vasculature," said Madri. "The vasculature of the yolk sac, which is important for nutrient, gas and waste exchange in the developing embryo, was arrested when the glucose level was high." What's more, glucose levels didn't have to remain high for long to cause serious problems, the research showed. Even a brief spike could be enough to abort a pregnancy.

In the newer work, published in the February 17 issue of *The Journal of Cell Biology*, Madri, Pinter and co-workers focused on a slightly later stage of development, when the cardiovascular system begins to form. Normally, this is a multistep process involving the endocardial cushion, a small area in the embryonic heart with two tissue layers, the endocardium and the myocardium.

"For normal development, endocardial cells overlying the cushion area have to dissociate from one another and migrate into the tissue beneath the endocardium called the cardiac jelly," said Madri. To investigate how the

process is disrupted under high-glucose conditions, the researchers used an *in vitro* model of endocardial cushion formation. With this model, they showed that high glucose levels inhibit dissociation and migration of the endocardial cells and that this disruption occurs during a critical window at the developmental stage when the embryo consists of 20 to 25 somites (block-like segments of tissue). Next, they explored the role of a regulatory molecule that is involved in keeping the cells in a sheet-like layer. In normal development, levels of platelet endothelial cell adhesion molecule-1 (PECAM-1) drop in the endocardial cells overlying the cushion area, allowing the endocardial cells to move apart and migrate into the cardiac jelly to form such structures as the valves and part of the walls between the chambers of the heart. But when glucose levels are elevated, PECAM-1 persists, the researchers found.

"The endocardial cells can't dissociate from each other and migrate," said Madri. "The result is a heart with an opening between chambers or one in which there are problems with the structure of the valves."

Why does PECAM-1 persist when glucose levels are high? The research implicates vascular endothelial growth factor A (VEGF-A), known to be important in the development of new blood vessels and the regulation of associated processes. Typically in diabetic adults, VEGF-A levels rise along with glucose levels. But for reasons Madri, Pinter and co-workers don't yet understand, in fetuses VEGF-A shows the opposite effect—its levels drop when glucose is high. Because VEGF-A affects the regulation of PECAM-1, low VEGF-A levels mean that PECAM-1 isn't properly controlled, allowing it to overstay its welcome.

Now, said Madri, "we're trying to understand how VEGF is controlled in the fetus and how that's different than in the adult. Once we know this, perhaps we can devise modalities to blunt the effect of excess glucose in the fetus."

—Nancy Ross-Flanigan

From the stomach to the brain: how a peptide hormone sparks appetite

In recent years neurobiologists have taken a keen interest in a peptide hormone called ghrelin. The molecule appears to be involved in activities such as growth hormone release, energy homeostasis and the functioning of the cardiovascular system. Big Pharma sees in it a potential target for diet drugs because of its role in sparking an appetite.

It is also of interest because, although it is produced by the stomach, it is found in the hypothalamus as well. Now researchers at Yale have tracked ghrelin to a group of previously uncharacterized neurons in the brain's appetite center.

"Ghrelin-producing cells are distributed in the hypothalamus in such a

manner that they are in a perfect position to coordinate the activity of the different hypothalamic subnuclei already known to regulate daily energy balance," said Tamas Horvath, PH.D., D.V.M. senior author of an article in the February 20 issue of *Neuron* and associate professor of obstetrics and gynecology and neurobiology.

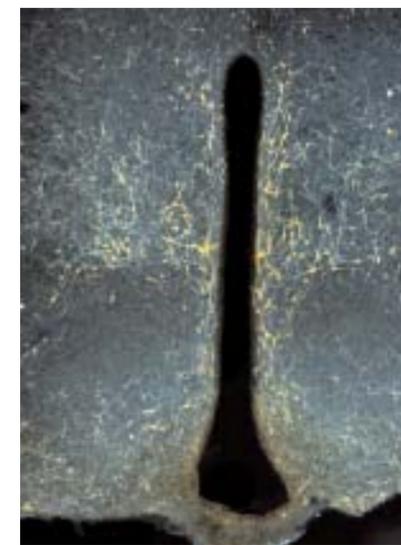
Studies in rats and humans had already shown that ghrelin signals the brain's appetite center when energy levels are low. Levels of ghrelin rose before and declined after meals. The mapping of the ghrelin circuit to neurons in the brain offers a new target for regulating appetite and food intake, Horvath said.

"We believe that these neurons are conveying information regarding circadian rhythm and sensory clues as well," he said. "You could be watching a movie, see food and become hungry, or be in the kitchen and smell something and become hungry, even if your stomach is full. These brain ghrelin neurons may be those that enable these brain processes to dominate over the actual need for energy intake."

One hypothesis, Horvath said, is that the system that balances food consumption, energy expenditure, body weight and fat stores may be suppressed by events such as stress or pregnancy. The neuronal system that signals olfactory and visual clues would then dominate.

"We are now working to find out how ghrelin from the stomach and from the brain work together or independently to regulate appetite or food intake and other brain mechanisms," Horvath said.

—John Curtis



A cross section of the hypothalamus shows ghrelin neurons and axons, in yellow. These molecules coordinate processes including appetite.

TAMAS HORVATH

et cetera ...

A DNA "MIMIC" TO REPAIR GENES

A peptide nucleic acid (PNA) that mimics DNA holds the promise of repairing defective genes, according to Yale radiologists and geneticists.

PNA, which replaces DNA's phosphodiester backbone with a polyamide one, creates a strong bond with DNA, said Peter M. Glazer, M.D., PH.D., professor and chair of the Department of Therapeutic Radiology. "If you can bind something to the gene, maybe you can use that to change the gene," he said. "If you change the gene to a new sequence it is permanently fixed."

In a study published in December in the *Proceedings of the National Academy of Sciences*, Glazer, the senior author, described the use of PNA to introduce a specific DNA sequence into a target gene in extracts of human cervical cancer cells. The new DNA sequence corrected a mutation in the target, the authors reported.

PNA, they concluded, could serve as a tool both for research and for repairing genes implicated in hereditary diseases such as sickle cell anemia and cystic fibrosis.

—John Curtis

BOOST FOR PROTEIN, GENE STUDIES

The Center for Genomics and Proteomics, founded last year with a \$200 million investment from the university, awarded \$300,000 in seed money this winter to seven groups of scientists on Science Hill and at the medical school.

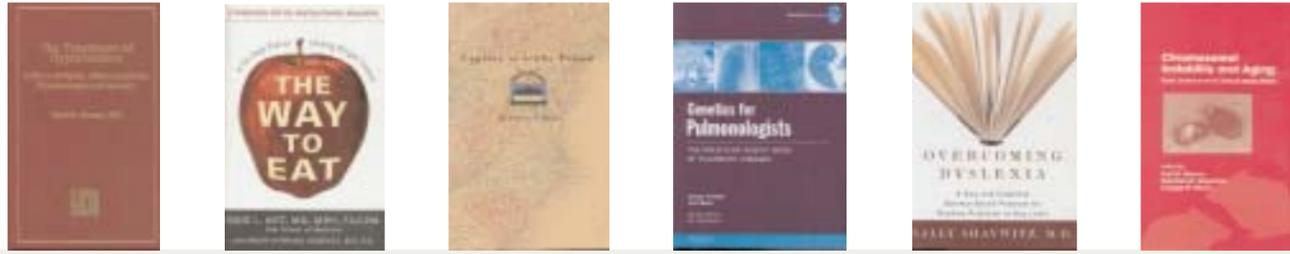
"We were looking for projects which have prospects of developing into large programs," said Sherman M. Weissman, M.D., Sterling Professor of Genetics and professor of medicine, co-director of the center. Michael Snyder, PH.D., the chair and Lewis B. Cullman Professor of Molecular, Cellular and Developmental Biology, is the director of the center. The funded projects will include research in lipids, *Arabidopsis* proteome chips, genomic microarrays in *C. elegans* and *Drosophila*, a cryopreservation facility and profiling of the rice genome.

"The pilot grants are a great way to stimulate integrative and cutting-edge research projects for the center," said Snyder.

—John Curtis



THE SWEDISH SEA, CENTER PANEL BY JIM DINE
GESM-ED MENEELY / ART RESOURCE, NY



The Treatment of Hypertension: A Story of Myths, Misconceptions, Controversies and Heroics, 2nd ed.

by Marvin Moser, M.D., clinical professor of medicine

Le Jacq Communications (Darien, Conn.) 2002

Moser focuses on the devastating consequences of untreated hypertension. Management of this public health problem has evolved over the past century; hypertension was once considered to have beneficial effects on health since the higher the pressure, the better the circulation. This rudimentary misdiagnosis along with other myths and misconceptions regarding the treatment of hypertension are discussed and debunked by the author.

The Way to Eat: A Six-Step Path to Lifelong Weight Control

by David L. Katz, M.D., M.P.H. '93, associate clinical professor of public health and medicine, and Maura Gonzalez, M.S., R.D.

Sourcebooks Trade (Naperville, Ill.) 2002

This book offers a comprehensive overview of food and diets, beginning with a guide to nutritional basics and what people need to eat vs. what they may want to eat. While not offering a specific diet plan, the book provides practical tips and persuasive reasons for changing eating habits.

Captive of Libby Prison

by Stewart J. Petrie, M.D., HS '55
Pentland Press Inc. (Raleigh, N.C.) 2002

Petrie has captured a side of the Civil War that is not often portrayed: a personal perspective. Fighting for the Union Army during the Civil War, Charles Robinson—Petrie's great-great-uncle—wrote home frequently to friends and family describing the battle being fought around him. He and the other men in his regiment were captured by Confederate soldiers and held in the notorious Libby Prison. These personal accounts describe a far different war than the one often portrayed by military strategists.

Genetics for Pulmonologists: The Molecular Genetic Basis of Pulmonary Diseases

by Jordan Prutkin, M.D. '02, Joel Moss, M.D., and Eli Hatchwell, series editor

Remedica Publishing (Lincolnshire, Ill.) 2002

Genetics for Pulmonologists provides an overview of lung diseases whose genetic defect has been defined as of June 2001. It is an easy-to-use manual with concise reviews of genetic diseases that a pulmonologist might encounter.

Overcoming Dyslexia: A New and Complete Science-Based Program for Overcoming Reading Problems at Any Level

by Sally Shaywitz, M.D., professor of pediatrics and in the Child Study Center

Alfred A. Knopf (New York) 2003

This comprehensive book helps us understand, identify and overcome the reading problems that plague American children. Shaywitz's book corrects such popular myths as the beliefs that dyslexia is primarily a male problem, that children with dyslexia see words backwards and that dyslexia is linked to intelligence. She shows that although dyslexia cannot be outgrown, its effects can be overcome with careful planning and hard work.

Encyclopedia of Psychotherapy

edited by William H. Sledge, M.D., FW '75, professor of psychiatry, and Michel Hersen, M.D.

Academic Press (San Diego, Calif.) 2002

This two-volume set covers the major psychotherapies currently in practice as well as the classical approaches that laid the foundation for the various contemporary treatment approaches. In addition, it identifies the scientific studies conducted on the efficacy of the therapies and reviews the theoretical basis of each therapy.

Chromosomal Instability and Aging: Basic Science and Clinical Implications

edited by Fuki M. Hisama, M.D., HS '92, assistant professor of neurology, Sherman M. Weissman, M.D., Sterling Professor of Genetics and professor of medicine, and George M. Martin, M.D.

Marcel Dekker Inc. (New York) 2003

Understanding the biological basis of aging is increasingly important as we anticipate the impact that a rapidly growing older population will have on the medical and social landscape. This book provides readers with background information on the biology of aging and the genetic alterations and epigenetic remodeling that occur with normative aging. It brings together expert reviews on the cellular and molecular bases of chromosomal instability and aging in human diseases and animal models, cellular senescence, telomeric regulations and oxidative stress.

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



JULIA GREENSTEIN

From pigs, the possibility of replacement tissue

With donor organs unavailable for most of the 80,000 people awaiting transplants in the United States, scientists are working to overcome the two biggest hurdles to xenotransplantation—immune rejection and infection. A Massachusetts company, Immerge BioTherapeutics, in collaboration with researchers around the country, has eliminated a gene in a cloned “knockout” pig that produces a key enzyme in the rejection process. The company has also identified swine that do not produce porcine endogenous retrovirus, which has been found to infect human cells *in vitro*.

“The waiting list for transplants continues to grow,” Julia L. Greenstein, PH.D., president and CEO of Immerge, said in a January talk sponsored by the Interdepartmental Program in Vascular Biology and Transplantation. “For the most part the donor list has remained incredibly static. We need to be able to do something else to address the patients who are on the waiting list and are never going to get organ transplants.”

—John Curtis



TOMAS LAGERWALL

An advocate for access, for all

As a child Tomas Lagerwall paid a visit to a “cripple center” in his native Sweden. “I remember seeing all those people sitting in wheelchairs doing nothing,” said Lagerwall, secretary general of Rehabilitation International, a network of more than 230 organizations in 90 countries devoted to promoting the rights of the disabled.

But over the years attitudes toward people with disabilities have changed, Lagerwall said at a talk at the School of Public Health in January. The 19th-century notion of institutionalizing them fell by the wayside as people with disabilities became more independent and capable of negotiating the outside world. “Today we talk about disability rights and an inclusive society,” Lagerwall said.

To that end Rehabilitation International is promoting a UN Convention on the Rights of People with Disabilities as well as community-based rehabilitation (CBR), which provides cost-effective programs in developing countries where at least three-quarters of those with disabilities live. “The CBR concept is that two-thirds of the rehabilitation work can be done at the local level, with local staff. It does not have to be very costly.”

—John Curtis



DANIEL SULMASY

In medicine, a spiritual crisis

Medical science has, in the last century and a half, permitted miracles unimaginable in the day of Hippocrates, says Daniel P. Sulmasy, M.D., PH.D., a Franciscan friar and director of the Bioethics Institute of New York Medical College. Yet, he says, physicians are among the most dissatisfied of professionals. The science and economics of healing, he told an audience at the Program for Humanities in Medicine Lecture Series in January, have dehumanized medicine. “I believe people are reaching a point which is very close to crisis,” he said. “I believe the crisis is primarily a spiritual one.”

Illness, he said, is a disruption of relationships within the body. Healing is the art of restoring “right relationships.” That requires more than a seven-minute office visit, with referrals to unknown specialists or prescriptions for medications limited to those on an HMO's approved list. It requires a strong relationship between physician and patient. “What is the meaning of medicine? What is its value? What are right and good healing relationships about?” he asked. “Those are spiritual questions.”

—John Curtis



AMY ZELSON MUNDORFF

Giving names to the dead in the wake of 9/11

As the Office of the Chief Medical Examiner in New York City began processing the victims of 9/11, a fundamental decision about the massive operation was made. “No autopsies were going to be done,” said Amy Zelson Mundorff, M.A., a forensic anthropologist with the city. “The cause and manner of death were not at issue.”

Instead, Mundorff said at a pathology grand rounds in February, identification was the main concern. A “rule of thumb” quickly emerged: any human fragment bigger than a thumbnail would be DNA tested. DNA testing determined the identities of more than 5,000 of the 20,000 fragments found. The medical examiners also used dental records, clothing, personal effects, tattoos and prostheses to identify 1,480 of the 2,792 victims. They still have hopes of someday identifying all the victims.

“Our chief has promised the families it will never be over,” Mundorff said. “Even though we have done all the identification that we can from the information that we have, if new technologies come up in the future we can exhume and retest the unidentified pieces, if requested.”

—John Curtis

A new space for science

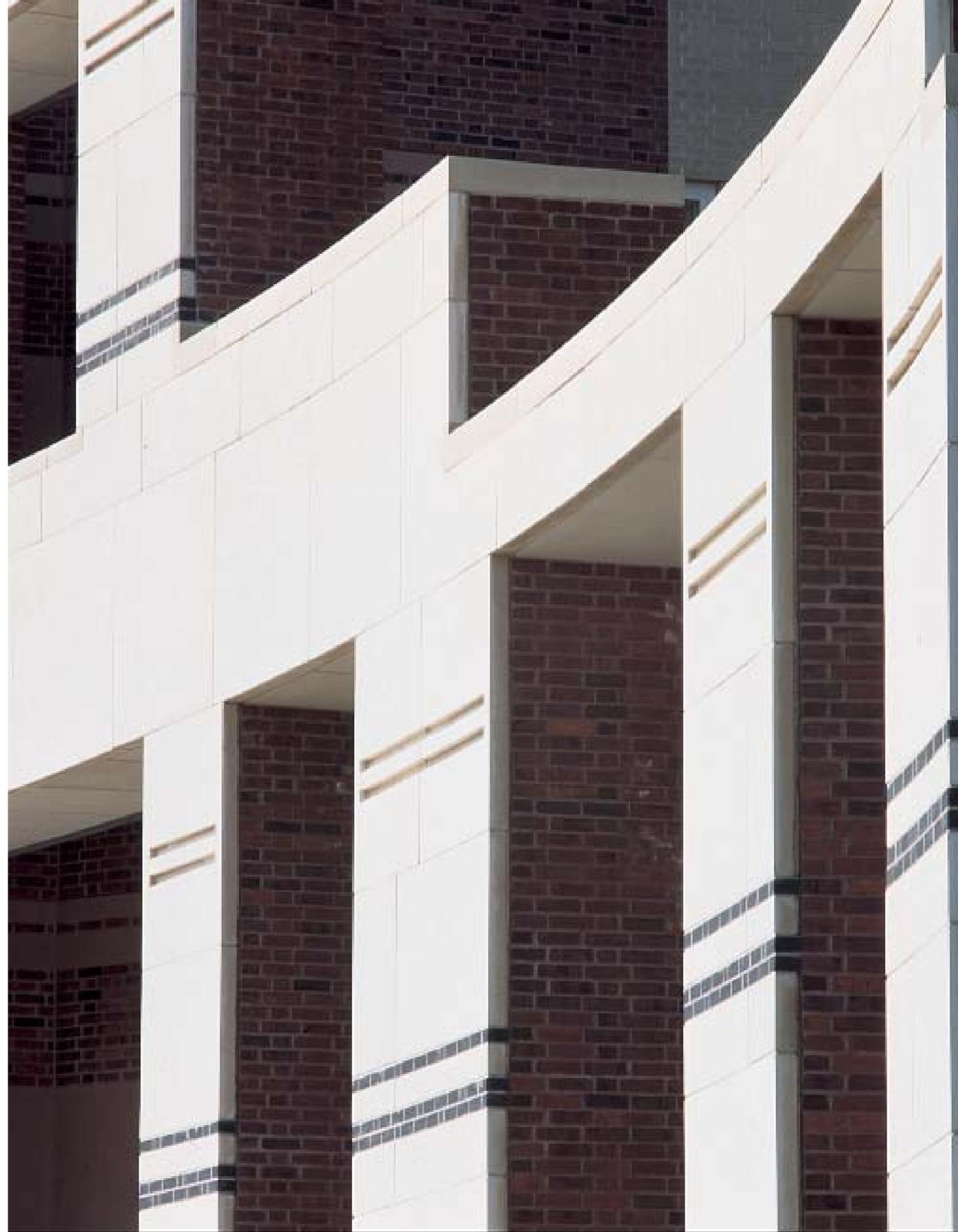
With the opening of The Anlyan Center for Medical Research and Education, the school dedicates its largest building ever.



TERRY DAGRADI

ABOVE Betty Jane and John Anlyan, accompanied by President Richard Levin, then-Dean David Kessler and New Haven Mayor John DeStefano Jr., cut the ribbon at the dedication of The Anlyan Center for Medical Research and Education in May.

RIGHT Detail from the entrance to the Anlyan Center.



FRANK POOLE



TERRY DAGRADI

“The architecture of a building is a statement about the culture of the institution,” Elias Zerhouni, director of the National Institutes of Health, said in his keynote address at the dedication. “The culture of research has changed at Yale.”

When A. John Anlyan, B.S. '42, M.D. '45, arrived at the School of Medicine for first-year classes in the early 1940s, the corner of Congress Avenue and Cedar Street was home to the nursing dormitory and down the block from a few restaurants, a bar and not much else.

New Haven has changed since Anlyan's medical school days, perhaps no part of it more than this intersection and the city block that is bounded by Congress and Howard avenues and Cedar and Gilbert streets.

When Anlyan and his wife, Betty Jane Anlyan, visited New Haven in May for the dedication of the medical school's newest building, they saw the transformation firsthand. The new 457,000-square-foot complex occupying the block today, which combines facilities for research, education, magnetic resonance imaging and the care of laboratory mice, is the largest building ever constructed at the School of Medicine.

The Anlyans, who were early supporters of the project and had funded the building's education wing, decided during their visit to increase the amount of their donation significantly. In recognition of their generosity, the building has been named The Anlyan Center for Medical Research and Education. As President Richard C. Levin said in thanking them for their support, “No one has done more to assure the future of these endeavors at Yale than John and Betty Anlyan. Their gift has been integral to the realization of the vision for this building.”

A gala celebration

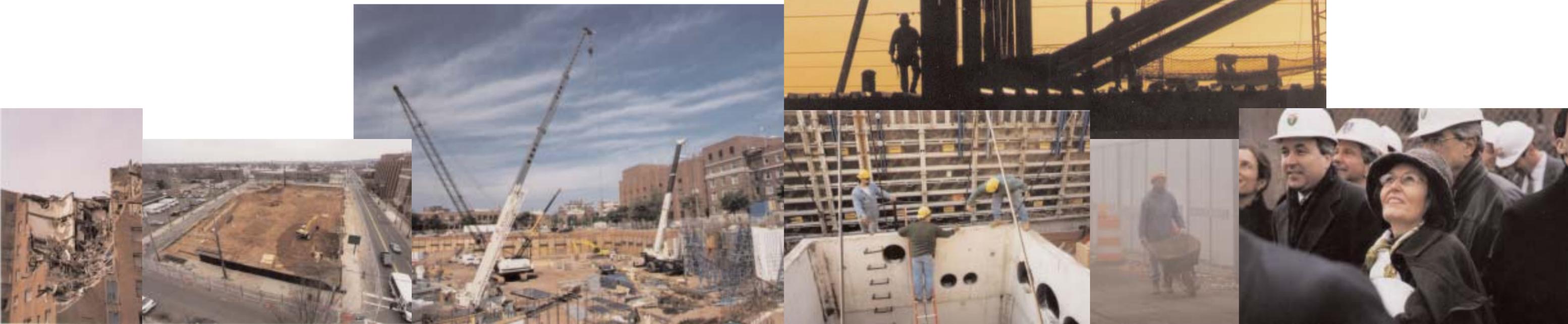
The building was dedicated on May 2 at a gathering of university and civic leaders, faculty members and alumni. Then Dean David A. Kessler, M.D. [See “From the Editor,” p. 3], called the \$176 million structure, which will be home to some 700 investigators, “the manifestation of Yale's vision for scientific collaboration, the study of human biology and educational excellence.”

Joined by several hundred guests including the director of the National Institutes of Health (NIH), Kessler predicted that the building would foster interdisciplinary collaborations among basic and clinical investigators and contribute to a “re-engineering of the clinical research enterprise ... that brings bench discoveries to the bedside.” President Levin—joined on the podium by university officers, New Haven Mayor John DeStefano Jr., the Anlyans and other major donors to the project—noted that the building constitutes the largest single investment in a building in Yale's history. In addition to thanking the Anlyans, he acknowledged the significant contribution of The Starr Foundation, a leading funder of medicine and health care worldwide, which is recognized in the naming of the C.V. Starr Atrium. Levin also thanked the W.M. Keck Foundation for helping to fund the 4-tesla magnet in the W.M. Keck High Field Magnetic Resonance Laboratory and the Howard Hughes Medical Institute (HHMI) for its ongoing support



FROM LEFT Before construction there was demolition. In January 2000 a wrecking ball began tearing down a former administrative building on Congress Avenue that had once been a dormitory for nursing students. By March the site, a block bounded by Congress and Howard avenues and Cedar and Gilbert streets, had been leveled in preparation for excavation and the laying of the foundation. Crews next began pouring walls and footings. Summer brought more cranes, dump trucks and cement mixers as walls started to rise. In the fall the building's skeleton took shape as steel workers laid beams. Project manager Reyhan Larimer and colleagues watched in March 2001 as workers “topped off” the building with its last piece of structural steel.

Photographs by John Curtis





Denise Scott Brown and Robert Venturi, of Venturi, Scott Brown & Associates of Philadelphia, designed the building in collaboration with Payette Associates of Boston.

for scientists at Yale, including HHMI investigators housed in the new building.

Big boost for science

In his keynote address, NIH Director Elias A. Zerhouni, M.D., underscored the importance of placing basic and clinical researchers in close proximity, as is the case in the new building. “We are in revolutionary times that require a change in the way we do research,” said Zerhouni, who encouraged scientists to “break the barriers between departments” by forming large teams that are truly interdisciplinary. In the teams Zerhouni envisions, scientists will not simply contribute expertise for a study directed by a colleague in another discipline, but rather will serve as equal partners, tackling “topics that cross diseases” and transcend departmental boundaries.

Zerhouni called the life sciences “the last frontier” and urged medical schools to “make it easy on the physicians to engage in clinical research. ... Young investigators need to be engaged early to enter biomedical research.”

The new building comprises six floors of laboratories, a three-story education wing for teaching anatomy and histology, a vivarium and greatly expanded facilities for magnetic resonance imaging research. The open spaces and large windows of the granite, brick and limestone building suggest a New England textile mill. The design and con-

struction process itself was a study in effective collaboration, said architect Denise Scott Brown of the firm Venturi, Scott Brown & Associates of Philadelphia, which designed the building with Payette Associates of Boston. When architects and builders collaborate with a client like Yale, they “embark on an adventure together,” Scott Brown said, “matching wits and building on each other’s ideas.”

Kessler noted that the completion of the building is “a step along the way,” part of a plan by Yale to invest \$500 million in the medical school campus over the next 10 years. “This building is a model we will use in the future to continue to transform the face of medicine at Yale.”

A lasting influence

Benefactor John Anlyan first came to New Haven from his native Alexandria, Egypt, in 1939 to attend Yale College and, later, the School of Medicine.

He trained in surgery at the University of Chicago Clinics and at Ohio State University while earning a master’s degree in enzyme chemistry. After returning to Yale as an instructor for two years and serving at Sloan-Kettering Institute in New York as a Damon Runyon fellow, Anlyan and his wife set out for California in 1954. For the next half-century, the couple devoted themselves to life in San Francisco, to his career as a cancer surgeon—and to Yale.

In recent decades, Yale presidents and deans visited the Anlyans’ San Francisco home, and the Anlyans retained a close interest in the university that educated John Anlyan and his two younger brothers—William, B.S. ’45W, M.D. ’49, who went on to become the chancellor of Duke University Medical Center; and Frederick, B.A. ’51, M.D., a Long Island pathologist. “I love Yale,” Anlyan said in June during a telephone interview from his new home in San Rafael, Calif. “It would never occur to me to do anything else but support it.”

But John Anlyan is not finished giving.

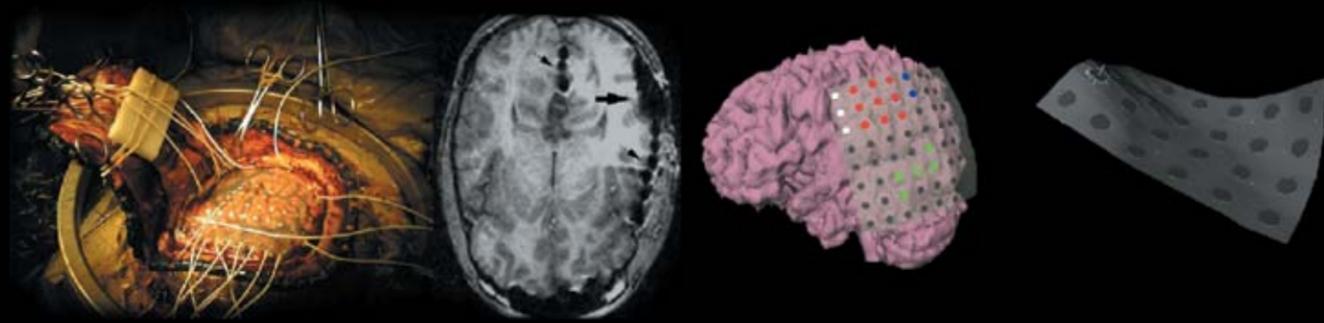
He has also willed his oil paintings of San Francisco scenes to the school, to be hung in the dissection room. It turns out that Anlyan, who speaks 10 languages and studied law in his spare time, isn’t a bad artist, either. “I think they’ll make it a happier place.” **YM**

FROM LEFT In January 2001, a year after demolition began, workers were pouring concrete floors in the building’s north wing. Meanwhile, on the ground below, numbered steel beams awaited placement. By summer the building was sheathed in scaffolding as workers finished the building’s “skin” of granite, limestone and 560,000 bricks. Inside the building’s two wings, finishing work—installation

of cabinetry, electrical wiring, plumbing, duct work and heating and air conditioning—continued. July 2001 marked a milestone with the completion of “mechanicals,” and two weeks later interior walls were rising. By summer 2002 the building was ready for testing of electrical, heating, air conditioning and air filtration systems. The final step was customizing the building to accommodate laboratory needs.



High resolution



The opening of a new Magnetic Resonance Research Center gives Yale expanded capabilities for advancing imaging science and disease understanding. Improving epilepsy treatment is just one focus.

By Marc Wortman

A quarter-century of progress

1979

Robert Shulman joins faculty

Robert G. Shulman, PH.D., who had pioneered usage of nuclear magnetic resonance spectroscopy (MRS) in combination with carbon isotopes to follow cellular metabolic pathways, joins Yale's Department of Molecular Biology and Biophysics from Bell Labs.

1983

MRS brain studies

The first proton and carbon MRS studies of the brain are performed at Yale, demonstrating the technology's potential to explore brain metabolism.

1986

MRC opens

With its first magnet for human subjects, the School of Medicine opens the Magnetic Resonance Center (MRC) in Fitkin Memorial Pavilion basement. Shulman directs the research portion and Richard H. Greenspan, M.D., chair of diagnostic radiology, directs the clinical portion. The MRC's two original magnets are still in use.

Amy Taylor (not her real name), a 30-something mother of two with a palm-size opening in her skull, tries to muster a smile as she sits up in a bed in the epilepsy monitoring unit at Yale-New Haven Hospital. A grid of depth electrodes penetrates the lumpy wet crown of her exposed neocortex. More than a dozen wires lead to a computer waiting to register the electrical firing patterns of the next in what has become a regular but unpredictable series of epileptic seizures.

The medications she has been taking for more than a decade no longer control those seizures, which are the result of temporal lobe epilepsy. She cannot work or drive, and rarely leaves home anymore. She will remain in the unit for up to 10 days, until enough data have been collected to localize the source of the malfunction in her brain. Electrical stimulation will also be fed into the electrodes while she undergoes a battery of tests to determine the precise location of critical language, movement and sensory areas.

Despite her present misery, she is fortunate. Hers is the only type of chronic brain disease that can be cured with surgery. But only the results of the tests will reveal whether she is a candidate for treatment.

Two to three patients each month undergo intracranial surgery for the type of testing Taylor underwent at Yale as a first step toward surgery to cure her epilepsy. The Epilepsy Education Association estimates that 20,000 Americans with intractable seizures could be cured with surgery, yet each year only 500 undergo the procedure. Fear and expense keep many patients away. Altogether, the procedure can cost more than \$120,000. Using new imaging technologies, Yale scientists hope to make the choice of surgery far less frightening and more economical. A mul-

OPPOSITE Using depth electrodes to record brain activity, neurosurgeons are able to locate and remove the tissue responsible for epilepsy while leaving critical brain regions unharmed. Yale scientists are now refining the procedure, using magnetic resonance imaging to reach the same outcome faster and less invasively. The sequence of images at left shows the process by which the electrode data are compared to three-dimensional MR data during development of the new system.

tifaceted team of engineers, linguists, physicists, neurologists, neuroscientists, applied mathematicians, computer scientists and neurosurgeons is refining methods for applying emerging magnetic resonance imaging (MRI) and spectroscopy (MRS) technologies to epilepsy. If they succeed, sometime within the next five years they will be able to locate the seizure focal point in a patient's brain and map out areas of brain function in less than three hours—a tiny fraction of the 10 days Taylor spent under observation—and without opening the skull. Just eliminating that part of the surgical process will reduce both the total cost of epilepsy surgery by up to 40 percent and a source of enormous fear for patients.

The Yale investigators' ambitions run well beyond that. They hope that sometime within the coming decade temporal lobe epilepsy will be curable without any surgery at all. According to Taylor's neurosurgeon, Dennis D. Spencer, M.D., HS '76, "It all hinges on our being able to use magnetic resonance imaging machinery to measure what's happening in the human brain."

New windows, new insights

Spencer, director of the Epilepsy Surgery Program at Yale and chair of the Department of Neurosurgery, already relies on MR studies to help guide him when he operates. The possibilities for developing treatment methods that, according to Spencer, "will put me out of business" depend on studies under way at Yale's Magnetic Resonance Research Center (MRRC). Already one of the world's leading scientific research programs of its kind, the MRRC received a major boost last winter with the opening of its new home in the 457,000-square-foot Anlyan Center for Medical Research and Education.

R. TODD CONSTABLE AND JAMES S. DUNCAN

1987

MRI group formed

Diagnostic radiology faculty launch research program aimed at the development of new approaches to magnetic resonance imaging (MRI) and improving the understanding of contrast mechanisms in MRI.

1988

Crossing to humans

The first MRS spectra of glutamate in the human brain demonstrate that information similar to that gleaned from previous animal studies could be obtained from the human brain.

1990

Glycogen synthesis in diabetes

MRS studies show that metabolic impairment of muscle glycogen synthesis leads to elevated post-meal blood glucose in non-insulin-dependent type 2 diabetes. This is first use of MRS (and of noninvasive imaging in general) to establish a fundamental mechanism in the etiology of a disease, and it paves the way to many pioneering studies of mechanisms of diabetes.

1991

MR for brain function

Lactate, a substance sensitive to increased activity in the human brain, is shown to increase during visual stimulation. This first use of MR (imaging or spectroscopy) to study brain function leads to a major application of MRS and MRI in use today.



TERRY DAGRADI (2)



TOP The new Magnetic Resonance Research Center includes a 4-tesla magnet for human studies that can pinpoint functional activities in areas as narrow as 500 micrometers.

ABOVE Center directors Rothman, left, and Constable, right, and collaborator Duncan.

The MRRC's 50-member staff, along with six multiton magnets supported by banks of computers, relocated from the Fitkin Memorial Pavilion basement to more than double the space in a two-story facility in the Anlyan Center (See "The Big Move," Winter 2003). On the upper floor of the new facility, faculty and administrative offices surround a large, light-filled open work space with computer workstations at its center. The facility has 40 networked computers dedicated to analyzing data produced by its magnets. At the computers, students and other investigators manipulate images of organs and graphic displays of data and develop algorithms to model the behavior of parts of atoms within cells.

For the faculty and staff, the new quarters represent the increasing importance of imaging technology to biomedical science and health care—and a big boost for morale. Director Douglas L. Rothman, PH.D., professor of diagnostic radiology, notes that this is the first time he has had a window in his office since he came to Yale as a graduate student in 1985. More important than what he can see out the window is what the new facility will enable imaging scientists to see at the molecular level. "This," he says, "is one of the best facilities in the world now."

On the floor below, the MRRC houses eight magnets, including two newly purchased systems. The MRRC maintains three animal and tissue research systems, including a soon-to-be-installed 11.75-tesla animal magnet, able to measure changes in animal metabolism at the molecular level. (A tesla, named for radio-engineering pioneer Nikola Tesla, is a measurement of the strength of a magnet's field.) The center also houses three human systems, including a new 4-tesla functional MRI (fMRI) system in the W.M. Keck High Field Magnetic Resonance Laboratory that can pinpoint functional activity in an area as small as 500 micrometers across. That is half a millimeter, about the size of the fundamental information processing units in the human brain (often referred to as cortical columns).

The state-of-the-art, \$3.7 million human magnet was paid for in part through a \$1 million grant from the W.M. Keck Foundation. There are also empty bays waiting for eventual installation of two additional magnets. All of the MRRC bays are encased within 11 inches—nearly 2 million

pounds—of steel and copper to shield out even the most minute radio signals, which could wash out reception by the ultrasensitive magnets, and to contain their magnetic fields.

The new magnets have already dramatically improved what investigators will be able to visualize. Studies of the central nervous system will benefit particularly from the magnets' higher sensitivity. "They allow us to look at fundamental neuronal processing units, which we could not do with our previous equipment," says Rothman. For instance, tissue that causes epileptic seizures can now be studied to determine precisely how metabolic processes critical to normal neuronal activity have malfunctioned, information crucial to the development of new treatment methods.

Seeing deeper

MRI and MRS studies in many fields at Yale, including reading and dyslexia, substance abuse, diabetes, mental illness and cardiovascular medicine, are providing methods for tracking down disease mechanisms and leading to novel forms of treatment. Basic science research at the MRRC is contributing to a new understanding of fundamental physiological mechanisms such as how energy is metabolized in the brain, heart and muscles. MR physicists at the center have also expanded the understanding of the underlying physical principles of MRI and MRS.

The MRRC is both a core center serving the research needs of the entire university and the primary research space for seven Yale faculty. These faculty have primary or secondary appointments in the Section of Biomedical Imaging in the Department of Diagnostic Radiology, which was formed to synergize the expertise of the imaging research groups at the School of Medicine. About 50 separate grants, totaling nearly \$35 million and representing 50 faculty members in 13 different departments, rely upon the MRRC. The center itself is supported by fees from those grants and \$7 million in direct research grants to faculty in the Section of Biomedical Imaging. The section is linked to the Department of Biomedical Engineering, which is part of both the medical school and the Faculty of Engineering on the main campus. In 2002, the new National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health

awarded its first-ever grant to the section, \$1.3 million to develop technology to map neocortical epilepsy.

Faculty and staff at the MRRC work on their own research advancing imaging science and also devise new ways to apply imaging technologies to biomedical problems. "We're developing state-of-the-art magnetic resonance techniques," says R. Todd Constable, PH.D., associate professor of diagnostic radiology and neurosurgery and director of the fMRI group at the MRRC, "and as a function of that we're able to provide a state-of-the-art resource for the whole university."

MRI is a complex technological feat, combining physics, mathematics, computer sciences and biomedical science. The hauntingly clear MRI pictures result from the differing radio signals given off by protons in the atoms of tissues exposed to the intense magnetic fields. Those signals must then be interpreted by computers and translated into graphic imagery. The MR data require extensive manipulation, particularly in complex experiments, to be translated into readable images. Rothman says, "Studies rarely work straight out of the can."

Constable and his 20-member team provide imaging support for more than 30 faculty members directing major grant-supported investigations utilizing fMRI within and outside the university. These include efforts to improve the understanding of autism with Robert Schultz, PH.D., in the Child Study Center; studies of the role of the frontal lobe in working memory and executive processing with neurobiologist Patricia S. Goldman-Rakic, PH.D.; mapping of memory processing with psychologist Marcia K. Johnson, PH.D.; and experiments aimed at finding better treatments for gambling disorders with Marc N. Potenza, PH.D. '93, M.D. '94, and for schizophrenia with Bruce Wexler, M.D., FW '77, both in the Department of Psychiatry.

One of the most active programs utilizing MRRC resources is the Yale Center for the Study of Learning and Attention, which has pioneered the study of pathways the brain uses for reading. Co-director Sally E. Shaywitz, M.D., also directs the Connecticut Longitudinal Study, which is investigating the development of reading skills in children from ages 7 to 18, and in adults, and is the largest MRI study ever undertaken in children. With the resources of

1992-1993

Cognitive fMRI

For the first time, functional MRI (fMRI) is proven able to measure single, brief, mental events without averaging across many seconds. The paradigm is now considered standard in many fMRI applications.

1993-1995

Measurement of GABA

Spectral editing in humans is developed and then used to demonstrate that MRS can measure the neurotransmitter gamma amino butyric acid (GABA). This opens the way to study alterations in GABA metabolism in neurological and psychiatric disease, starting with the observation that the mechanism of action of several anti-epileptic drugs is through elevation of cellular GABA.

1995

Sex differences in brain

fMRI reveals that women and men use different brain regions to process language. Results demonstrate more bilateral activation in women during word processing compared to generally left-brain activity in men. Research provides direct evidence that helps to explain why women are less likely to lose language capabilities after strokes.

Functional localization verified

Studies validate the emerging method of fMRI by demonstrating that areas found to activate in fMRI are representative of true functional areas. Results also demonstrate many additional systems involved in complex cognitive processing.

1996

Etiology of epilepsy

MRS is used to show that cellular GABA levels are low in epileptic patients with poor seizure control. This and subsequent studies have established low cellular GABA levels as a significant mechanism leading to cortical hyperexcitability in epilepsy.

1997

Reading and brain activity

Phonological effects are linked to printed-word identification and reading performance. Many studies in fMRI now equate brain activity with subject performance.

1999

Glutamate/glutamine cycle

First measurements of the glutamate/glutamine cycle, a direct measure of excitatory neurotransmission, are made in awake human subjects and show high rates. Results overturn the existing paradigm that the awake brain has minimal neuronal activity while resting. Findings suggest that, rather than waiting to be 'turned on,' the brain is constantly functioning in anticipation of stimuli.

GABA and psychiatric disorders

MRS data show that GABA metabolism is altered in depression. Subsequent studies show alterations in panic disorder, premenstrual dysphoric syndrome and alcoholism. Findings lead to a new appreciation of the importance of inhibitory neurotransmission and amino acid metabolism in psychiatric disease.

the MRRC, Shaywitz and her husband and research partner, Bennett A. Shaywitz, M.D., have mapped the neural systems responsible for reading. They have also begun to explore the impact on those neuronal pathways when educational techniques are used as interventions to help children with dyslexia overcome their reading challenges. “We can see how the brain is responding,” Bennett Shaywitz says of those education interventions. “If we see effects on the brain, we’ll know we’re on the right track.”

The Shaywitzes have begun to explore the use of MRS, a technique for measuring metabolic rates within tissue. The technique can measure the increased presence of a harmless biochemical tracer linked to glucose to show where increased or decreased metabolic activity, associated with tissue function, is occurring. The Shaywitzes will use MRS to search along the neural pathway for reading to find where disruptions underlying learning disorders may be taking place. “We are addressing questions at a finer and finer level,” says Bennett Shaywitz. By using the brain imaging technology they hope eventually to diagnose learning disorders early enough to prevent life-long difficulties.

Diabetes and brain energetics

Robert G. Shulman, PH.D., founder and for many years director of research in the MRRC and now Sterling Professor Emeritus of Molecular Biophysics and Biochemistry, oversaw installation of the first human-sized research magnet in Fitkin in 1986. He pioneered many of the MR techniques now used in biomedical research around the world. His work demonstrated the validity of MRS studies for tracing metabolism in tissue and then showed that the technology could be used to explore the role of metabolic pathways in humans. Many clinical advances followed those early studies.

In collaboration with professor of medicine and Howard Hughes Medical Institute investigator Gerald I. Shulman, M.D., PH.D. (no relation), Shulman showed that a defect in muscle storage of glycogen was responsible for the impairment exhibited by type 2 diabetes. That was in 1990. The following year, Robert Shulman, Rothman and James W. Prichard, M.D., a former professor of neurology

who is now retired, were the first to demonstrate the effectiveness of MR to follow brain functional activity, now a major application of the technology. Shulman also directed studies that proved the feasibility of using MR to study regional metabolic functioning in the brain.

Much about the brain remains a mystery, including how it utilizes energy to carry out its most complex functions. Robert Shulman, Rothman, and Fahmeed Hyder, PH.D., an associate professor of diagnostic radiology in the MRRC, have made a number of recent findings using MRS that have sparked an emerging re-evaluation of the nature of brain function. These findings were made possible by the development of MRS methods to simultaneously image brain energy consumption and the release of glutamate and GABA, the primary excitatory and inhibitory brain neurotransmitters, respectively. Their studies have shown that even at rest the brain uses 80 percent of its energy to support neuronal firing and neurotransmission, which are the bases of brain function. Previously it was felt that there was little neuronal activity in the resting brain.

Understanding the role of this enormous underlying activity has implications for brain function studies of all sorts. “The baseline is not negligible,” says Robert Shulman. Rothman adds, “Our brains are always ‘on,’ despite the high energy cost.” Understanding why this resting neuronal activity is necessary could help explain the complexity of higher-order brain functions, such as learning and memory, and potentially open up new pathways for understanding disruptions in those functions. “These results show that the popular analogy that the brain acts like a computer, which only accesses its processing power when it is called on to perform a task, is not correct,” says Rothman. “A new view of the cognition will need to account for the data.”

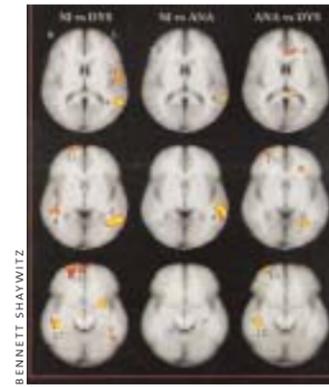
Back to the OR

Novel understanding of brain metabolism made possible by Rothman, Robert Shulman and others has radically altered neurosurgeon Spencer’s outlook on epilepsy and its potential treatment. Epileptic seizures are a state of electrical hyperexcitation that starts from a single site in the

brain and then spreads swiftly. Studies done at the MRRC demonstrate what Spencer terms a paradox. The focal point triggering the seizure is metabolically depressed relative to its surroundings. Spencer, Rothman and Ognen A.C. Petroff, M.D., HS ’82, associate professor of neurology, have been carrying out MRS studies to explain that paradox. MR analysis of tissue removed from patients with epilepsy showed that it was not processing glutamate appropriately. Instead, due to impairments in the cellular energy supply needed to keep extracellular glutamate at a safe, low level, the glutamate outside the cells was “backing up,” eventually setting off an electrical fluctuation that spreads quickly into a seizure. This and related findings may provide a key to treatment advances.

“This opened an important little door where we’ve not had many thoughts about new therapies,” says Spencer. “If it is an energy problem, then this is perhaps reversible.” Delivering medication to the site of the brain malfunction could reregulate the brain’s metabolism, much like pace-makers now do for patients with heart disease, to prevent seizures. Utilizing new technology in the MRRC, he says, “we can now create animal models to think about therapies. The underlying cause of epilepsy may be reversible, but the only way to know is by imaging before and after surgery.”

His work with the MRRC has already paved the way for better and potentially less-invasive treatments for epilepsy patients. In association with Spencer, the MRRC has developed new ways of bringing imaging techniques directly into the operating room. This summer, Spencer will begin operating on patients, utilizing computer-guided equipment developed by the Yale team in conjunction with the firm BrainLAB. He will operate while wearing goggles with a built-in monitor that gives him access to a virtual three-dimensional display of MR imagery from inside patients’ brains. The images, linked to the placement of the scalpel, will show him precisely where the cutting blade is located beneath the surface of the brain and what functional areas it is near. That should help reduce damage to surrounding tissue. Already he utilizes a portable version of the BrainLAB to give him visual information about the



BENNETT SHAYWITZ

Sally and Bennett Shaywitz have used functional MRI to measure differences in brain activity between groups of children with and without dyslexia. Colored areas in the images highlight locations in the brain where there is a marked difference in function in the two groups.

patient’s brain as he operates. “It looks just like a tricorder,” he says, referring to the medical device used in the futuristic television and movie series *Star Trek*.

James S. Duncan, PH.D., vice chair of diagnostic radiology and director of the Image Processing and Analysis Group, is helping to develop even more futuristic treatment methods. His group developed the software used to integrate spatial, functional and metabolic images recorded in MR studies into the real-time spatial coordinates of the patient’s brain as Spencer operates. He is also attempting to develop a model that simulates the natural deformation of the brain that takes place during open-skull surgery. “If you are off by even less than a centimeter, you can hit critical areas,” Duncan says. In the coming years, Spencer will use Duncan’s models of brain deformation while he operates. The two expect that, within the next five years, MRI and MRS testing to identify the source of seizures and map the functional areas of the brain in combination with Duncan’s graphic models will eliminate the need for the costly, arduous and potentially hazardous intracranial surgery that Taylor underwent.

Spencer credits the scientists at MRRC with changing his view of epilepsy. “Instead of thinking of epilepsy as an electrical problem,” he says, “I now think of it as a metabolic disease. They are much more than MR physicists. They make you think about disease-related problems in a different way.”

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

2000

Higher-order processing

Higher-order executive-processing regions in the brain are revealed for the first time, using fMRI, when subjects are asked to perform a dual task which requires focusing on some stimuli while ignoring others.

2001

Functional reorganization in brain

Studies demonstrate cases of true functional plasticity in the adult brain and characterize the reorganization observed as a function of a specific type of brain lesion (epilepsy, tumor, arterial venous malformation).

Bioengineering research partnership

A large NIH-funded project combines state-of-the-art imaging resources, research development and computer vision to improve treatment planning and understanding of epilepsy.

2002

Neurophysiological basis of fMRI

Quantitative fMRI methods are developed to map regional brain energetics directly. Further study shows that regional brain energy metabolism increases proportionately with neuronal firing during sensory stimulation in animal models, providing the first direct link between the imaging signal and electrical activity and opening up the possibility of using MRI to image brain function directly.

Differential processing of faces

Research demonstrates that autistic patients’ brains show similar activation patterns when processing pictures of objects and pictures of faces. Nonautistic control subjects activate a face-specific cortical region distinct from the object region when shown the same pictures.

Low birth weight and language

First study demonstrating not only structural but also functional differences between very-low-birth-weight infants and full-term infants.

A new home

The MRRC moves to a two-story, state-of-the-art facility in the new Anlyan Center for Medical Research and Education, uniting the MRS and MRI groups into one comprehensive center for magnetic resonance research.

— Marc Wortman
Sources: Douglas Rothman,
R. Todd Constable

SHOWDOWN
With WASHINGTON TACKLING
MEDICAL MALPRACTICE,
IT'S DOCTOR VS. LAWYER
IN THE COURT OF PUBLIC
OPINION. BY ELI KINTISCH

MELINDA BECK





When Ross M. Tonkens, M.D. '74, arrived in Las Vegas in 1990, the gold rush was on. Casinos were expanding, the work force swelled and doctors streamed into Nevada to serve a burgeoning local community. For five years Tonkens thrived in an independent internal medicine and cardiology

practice. "All a physician needed to succeed there was to be competent, caring and available," says Tonkens. Then, as he tells it, the lawyers arrived.

What followed was a nightmare. By last summer 58 orthopaedic specialists and vascular surgeons had walked off their jobs to protest soaring malpractice insurance rates—temporarily closing the trauma center at the University Medical Center in Las Vegas in the process. But even before that job action, Tonkens had faced a half-dozen lawsuits in the same number of years. One woman, with diabetes, sued him after her kidney failed. The suit charged Tonkens, at the time serving on his monthly rotation as admitting doctor in the emergency room, with "allowing" the patient to leave the hospital—even though Tonkens had advised against it, warning her that she could very likely lose a kidney if she did so. Indeed, the patient had even signed documents acknowledging her understanding of this warning.

The other lawsuits were similarly flimsy, and Tonkens had himself dismissed as a party or saw the cases thrown out. "Nevertheless, each suit cost me dearly in time lost from patient care," says Tonkens. "Every one of these was a 'pay me and I'll go away' extortion suit, with the plaintiff's attorney assuming I would rather settle than spend the time and money to defend myself." The pinnacle of Tonkens' legal skirmishes came when he found himself sued over his refusal to prescribe oral feeding and exercise to a comatose woman. The woman's son, who had filed the suit and had no heirs, later died, but the man's attorney refused to drop the case, claiming a "fiduciary duty" in the interest of his client's estate.

Among the first of the doctors who had come to Las Vegas at the beginning of the 1990s, Tonkens blames lawyers for his eventual retreat from Nevada. "In 2001, I was also in the vanguard, this time as one of the first physicians

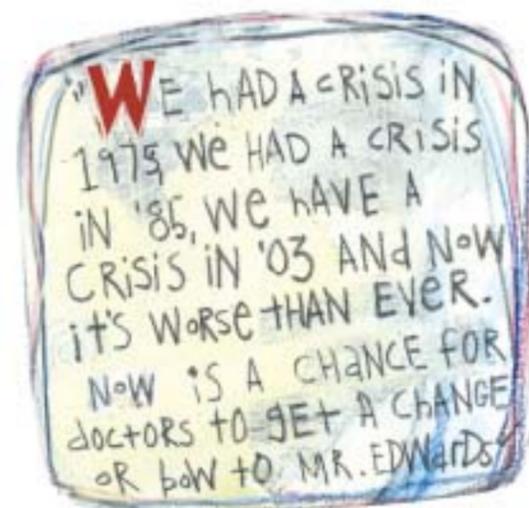
to flee the state because of legalized extortion by the onslaught of personal injury attorneys flooding into the malpractice arena," says Tonkens, who is now director of medical and scientific services at Quintiles Transnational Corp., a North Carolina-based pharmaceutical consulting firm.

Two views of the world

Tonkens' antipathy for attorneys reflects a growing tension in medicine, and one that has put doctors and lawyers at odds like never before. Already hurt by falling reimbursements from managed care and stung by the accompanying challenges to their professional autonomy, physicians now find themselves under assault on another front. Skyrocketing malpractice premiums are forcing doctors across the country to leave their practices; drop higher-risk specialties like neurology, obstetrics and orthopaedics; or move to states with more forgiving tort laws. Backed by President Bush and Senate Majority Leader Bill Frist, M.D., a Republican from Tennessee who is the first physician to lead the Senate, they blame lawyers for their woes and have pushed for reform in Washington and dozens of state capitals. At the top of the list when Bush made his State of the Union address last winter was a proposal for a \$250,000 cap on noneconomic damages in malpractice cases. That proposal passed the House of Representatives in March, but in July a Democratic filibuster squelched the bill in the Senate. Although national legislation is unlikely before the next election, Frist vowed that the issue "will be back." Several state legislatures may follow the lead of Texas, which passed a malpractice cap in June.



Has the malpractice issue hit home with doctors? Nearly 2,000 white-coated physicians rallied outside Connecticut's Capitol building in late March, the largest such gathering ever.



MELINDA BECK (3)

Trial lawyers insist that a cap would take away a malpractice victim's chance for recompense and that the soaring premiums are the fault of the insurance companies. The lawyers see themselves as protectors of patients—as well as scapegoats in the current debate—and show no signs of accepting a cap on damages. Mary E. Alexander, president of the Association of Trial Lawyers of America, sees a long struggle ahead. "We are at war," she told the group at its convention in February, referring not to the conflict with Iraq then looming but rather the political struggle ahead over tort reform. "President Bush has laid the gauntlet down."

The debate also promises to be an issue in the 2004 presidential race. Vermont governor and physician Howard Dean, M.D., a 1971 Yale College graduate, has said the matter should be left to the states, and Senator John Edwards, J.D., a former trial lawyer who has represented patients, is opposed to the reforms. How seriously does the White House take the threat of the clean-cut young senator? Bush delivered a major speech on malpractice last summer in Edwards' home state of North Carolina. Months later a White House official described a Washington speech by Bush on the issue as part of a "whack John Edwards day."

Sparring over malpractice is emblematic of a natural friction between the two professions that manifests itself in competitiveness, disagreement and, at times, even humor (apparently in proportion to the social status enjoyed by both professions; there is a reason *The New Yorker* magazine publishes books of lawyer and doctor cartoons, but none about civil engineers).

"There is a built-in adversarial relationship here," says Yale law professor Robert A. Burt, J.D. '64. "Lawyers in the malpractice area are always sniffing around for mistakes. Doctors are adverse to any outsider pointing out errors. Just being sued can be devastating for their sense of themselves as professionals."

The president of the Association of Yale Alumni in Medicine, Francis R. Coughlin Jr., M.D. '52, J.D., agrees. "For doctors it's not simply a business matter—it's an attack on their integrity," says Coughlin. As one who can view this debate from both sides, Coughlin sees the main problem as what legal economists call transaction costs. Litigation costs money—hourly fees for the defense lawyer, contingency fees for the plaintiff's lawyer, settlements, expert-witness fees, court costs, the costs of acquiring records from hospitals and physicians—that is drained from the health care system. Supporting that system, he says, are three related pillars; cost, access and quality of care.

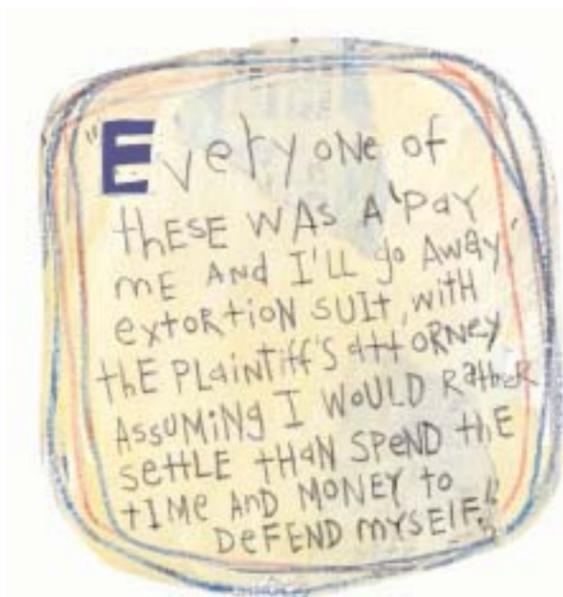
"The doctors want to provide access and they want to provide high-quality care, but money is going out of the system to fund transaction costs," Coughlin says, noting that, unfortunately, this is nothing new. "We had a crisis in 1975, we had a crisis in '85, we have a crisis in '03 and now it's worse than ever. Now is a chance for doctors to get a change or bow to Mr. Edwards, to whom trial lawyers are giving large sums of money to protect their own incomes. It's important that we get some input before the next presidential election."

At the core of the cultural divide between law and medicine are two often-conflicting world views—in particular, differing concepts of what certainty means in the context of medicine, says hematologist and ethicist Thomas P. Duffy, M.D. To Duffy, the expert-witness process, in which plaintiffs and defendants each call medical experts to testify on the medical procedure at issue, shows that attorneys see "truth" as that which can convince an uninformed jury. "That offends the whole authenticity of being a physician, which is predicated on telling the truth to your patients," says Duffy, a professor of medicine and director of the Program for Humanities in Medicine. "Without truth there is no science."

The last straw

Against this backdrop, the reaction of physicians to sharply rising insurance premiums has been almost visceral. In Ohio, West Virginia, New Jersey, Connecticut and elsewhere, physicians have protested on the steps of state capitals. The issue has stirred passions among Yale graduates in medicine and public health as well; more than two dozen alumni responded to an invitation from *Yale Medicine* to voice their opinions (See "On the Topic of Lawyers, No Shortage of Opinions," p. 32). Many took the time to explain at length how the crisis has affected their ability to care for patients, and where they think a solution may lie.

Tonkens, the former Las Vegas internist, was one of them; another was Edwina E. Simmons, M.D. '84, who started her own obstetrics and gynecology practice in Ohio in 2001. At that time, her malpractice insurance company quoted a rate of \$21,500 per year, going up to \$60,000 after



five years. But the rate reached \$60,000 after just two years. With a massive increase expected for this year, she left her practice to join a corporate multispecialty group, which pays for her insurance. “The entrepreneurial spirit of doctors has been shattered,” she says. “No longer can someone finish residency and hang out their shingle.”

When Harold R. Mancusi-Ungaro Jr., M.D. '73, HS '76, moved from Texas to California last year, he left behind a medical community that was fully preoccupied with the law. “The daily conversation in the doctors’ lounge and the weekly column in the local paper concerned who was being sued and by whom,” he says. Mancusi-Ungaro now works for Kaiser Permanente in Santa Rosa, Calif., where he says he can focus on patients and practice “the best medicine I’ve been able to pursue since leaving medical school.” He attributes the climate to the malpractice reform California enacted in 1975, which capped pain-and-suffering damages at \$250,000.

At times a truce

To portray doctors and lawyers as constant enemies would of course be misleading. While their lobbying proxies do battle in Washington and state capitals, most doctors and lawyers share a degree of empathy and admiration. And although Connecticut internist Sally R. Bergwerk, M.D., M.P.H. '98, says she does not admire lawyers who reap unseemly profit from injured patients, she does respect those who will take on only cases with credible and substantial allegations of negligence. For example, she says, the Bridgeport, Conn., law firm of Koskoff, Koskoff and Bieder is a name to take seriously.

“If you get a call from Koskoff, you should start to sweat, because you know it’s not frivolous,” she says. Koskoff senior partner Michael P. Koskoff, whose staff includes several Yale law alumni, says that the firm only takes 3 per-

cent of the patients who call looking to sue. California trial lawyer and malpractice specialist Joel W.H. Kleinberg, J.D. '67, performs a similar screening process. “Many times the half hour I spend explaining what has happened and why an unfortunate outcome doesn’t mean ‘malpractice’ is all that’s needed to dissuade an unhappy patient from suing.”

But building on trusted relationships to tackle malpractice reform won’t be easy. The current debate simply divides the two groups too bitterly, as the sides can’t even agree on how to refer to the problem: attorneys call the ongoing efforts a push toward “medical malpractice reform,” and spokespeople for doctors call the issue “liability reform” as a way, it seems, to avoid the M-word.

“I think liability limits on noneconomic damages are part of the solution. They seem to have worked in states like California,” says Robert M. Segaul, M.D., HS '72, who trained in urology at Yale. “There are severely damaged patients for whom this is not fair, but if the system is bankrupted and doesn’t operate for the majority of patients, then it needs to be implemented.” Lawyers, conversely, contend that some kind of limit on fees would only handcuff wronged patients. Led by Democrats on Capitol Hill, they accuse insurance companies of price gouging—and of using malpractice business to shore up revenues in the face of other losses in a down stock market.

“It’s the insurance business cycle that drives all this,” says Kleinberg. Holders of all types of insurance policies, say analysts, are affected when companies raise rates to cover deep investment losses. Trial lawyers want to pressure insurance firms by ending their long-standing exemption from antitrust laws. That, the lawyers say, would lead to more competition and lower rates.

The two sides also clash over the contingency system. Usually, malpractice attorneys aren’t paid unless they deliver a successful verdict or settlement. “The most-injured patients need the least work by lawyers, get the highest awards and reward lawyers with huge profits,” says Joe Bauer Jr., M.D., HS '57, who was a surgical intern at Yale. “These unjustified profits are unrelated to the legal work required and to the validity of the ‘malpractice’ and rob patients of the bulk of their deserved compensation. Lesser injuries require the most work, with less profit, and these patients are not helped and are ignored by lawyers.” He would also welcome a change in the process of designating expert witnesses. “Expert-witness designation, for plaintiff and defendant, must be made the function of a medical specialty board, and not be decided by a trial judge, who is usually not capable of assessing the appropriate medical qualifications of an expert medical witness,” he says.

But attorneys defend the contingency fee system as a mechanism that prevents frivolous suits. In addition, contend lawyers, only the possible reward of a large settlement motivates attorneys to take a risk on a case they

might lose. This doesn’t appease physicians like Bergwerk, who says that, “in Connecticut, of every dollar given as rewards in malpractice suits, only 42 cents goes to the patient.” That’s why on March 26, Bergwerk appeared with close to 2,000 other Connecticut doctors—the largest gathering of physicians in the state’s history—at Hartford’s statehouse to lobby for reform. Tim Norbeck, executive director of the Connecticut State Medical Society, says one of every three practicing physicians in the state attended the rally.

Fixing the system

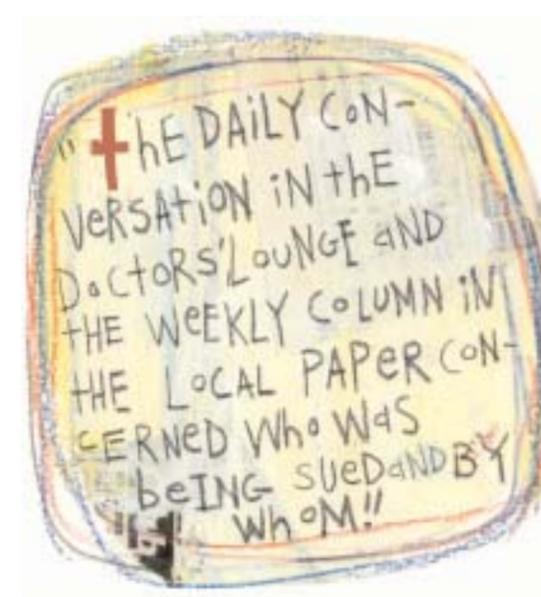
To some, framing the fight between doctors and lawyers as a crisis of lawsuits misses the supposed goal of the medical tort system: preventing the medical mistakes that plague American hospitals. “There is a lot of bad medicine out there in the real world,” says Mary Jane Minkin, M.D. '75, HS '79, a clinical professor of obstetrics and gynecology who has testified for years in malpractice cases on behalf of both doctors and plaintiffs. An oft-cited 2000 Institute of Medicine study estimated that as many as 98,000 patients die each year in American hospitals due to preventable medical errors. But deciding whom to blame is not the overriding issue. “Many suits do not involve malpractice—just maloccurrence,” says Minkin, “and many acts of malpractice do not end up in litigation. Our goal is the best medicine for all, with no malpractice, and no doctor sued for a bad outcome which was not his or her fault.”

Chris Cassirer, SC.D., M.P.H. '91, an associate professor of health care management at the University of Minnesota, has studied the problem for over a decade and agrees that



Among the Hartford marchers was Yale alumna Sally Bergwerk, a Fairfield County internist who laments the contingency fee system that governs the distribu-

tion of malpractice awards. “In Connecticut,” she says, “of every dollar given as rewards in malpractice suits, only 42 cents goes to the patient.”



improved prevention of injury should be the highest goal of any reform effort. Strong managers and open discussion of mistakes and ways to prevent them, he has found, are effective tools for minimizing errors. But, he adds, “there’s a great deal of concern that talking about a medical error after it occurs will lead to lawsuits instead of looking at the processes that led to the mistake and fixing what’s wrong.” Yet honesty may be the best policy for keeping patients from visiting an attorney in the first place. “People will tolerate a variety of mistakes and medical mishaps if you’re up front with them,” says Howard V. Zonana, M.D., HS '63, professor of psychiatry and adjunct clinical professor of law at Yale.

Doctors and lawyers both say the seeds of the misunderstanding are deeply planted. That’s the conclusion Robert J. Levine, M.D., HS '63, drew years ago while teaching an ethics class to first-year law and medical students at Yale. “We began with a discussion of justice. Everything went well for about 10 minutes until we got to the question of whether the system should be based on good procedures or good outcomes,” says Levine, professor of medicine and co-chair of the executive committee of the Yale Interdisciplinary Bioethics Project.

“A medical student said, ‘Of course the outcomes must be good or the system isn’t worthwhile.’ One of the law students disagreed immediately,” Levine recalls. “He said, ‘The procedures must be fair or the system is invalid. That’s why we let murderers go when the evidence is obtained illegally.’ For the lawyer, procedure is everything, but for a physician, if the patient doesn’t get better, what’s the point? Here they were in only their first year, and already they were that far apart.” YM

Eli Kintisch is a writer in Washington, D.C.

On the topic of lawyers, no shortage of opinions

Are attorneys to blame for doctors' woes? Well, yes, but there are more fundamental issues in the malpractice debate.

As the public dialogue about malpractice insurance reached a crescendo in February and physicians across the United States staged demonstrations for limits on lawsuits, we invited alumni in medicine and public health to share their opinions about the roots of the problem and its possible solutions. Readers of *Yale Medicine* were generous with their ideas; echoed in many of the messages is a sense among alumni that the business of medicine has chipped away at the doctor-patient relationship. Many also feel that, as a society, we look to assign individual blame for poor outcomes instead of attending to systemic flaws that could be repaired to improve medicine and prevent errors from happening in the first place. Here is a sampling of the responses we received.

Malpractice mess reflects a need to regroup

There are numerous factors that contribute to the current problems in malpractice suits and insurance.

There is no unified, cogent voice for physicians. The American Medical Association, once the most powerful lobby in Congress, was not supportive of Medicare and lost the prior uniform support of doctors. Today, the AMA has little impact on legislation or thinking about medical issues. The organizations of the various medical disciplines are too splintered to have an effective voice, although the American College of Surgeons has made an effort.

The image of the physician has sunk to unimaginable depths, partly because of unfulfilled expectations, partly due to actual malpractice and partly due to the depersonalization of medical care in the HMO/prepaid/group environment.

The tort lawyers are clever, successful and energetic. Their financial successes help to empower their voice in judicial appointments and in legislative action.

The advances in medicine and surgery have increased not only the horizon of treatable and preventable disease but also the risks, potential bad outcomes and severity of disease that is attacked.

Since the federal government encouraged the expansion of medical schools a few decades back, increased competition among physicians may be distracting some of them from seeking ideal patient outcomes.

Censure, reprimand and punishment of physicians for malpractice are accomplished by the competitive and antagonistic tort system, without a parallel goal of preventing further error and without any real effort to improve medical care.

It may be too late for the physicians to regain control; the hospitals have largely separated themselves from allegiance to the physicians. The HMOs are likewise unhelpful and the medical schools have been passive. Perhaps an independent commission should investigate the problem and make suggestions for its solution, either through meaningful legislation or some new national system aimed at both appraising suspected instances of malpractice and correcting the flaws and circumstances that lead to poor medical outcomes.

Robert C. Wallach, M.D. '60
New York, N.Y.

The big question: where to impose limits?

The hottest issue in this tempest is probably the perception of "open season on physicians" and on medical care in general. While many doctors may have been influenced in their ordering of diagnostic tests by the idea of defensive medicine, I believe the greatest damage that this produces is to the physician-patient relationship. An element of trust is gone. Is this a consequence or side effect of malpractice, or both? Why should it be socially permissible for lawyers to advertise "you may be entitled to a large cash award," reinforcing the perception that the absence of perfection in medical care entitles them to lottery-type winnings? While I am delighted that lawmakers, who of course are generally lawyers, are making some strides in malpractice reform, the controversy continues over just where limits should be ethically imposed. We need expertise and responsible leadership on this issue.

Marie Tsivitis, M.P.H. '86
Stony Brook, N.Y.

Michigan's specialty solution

The malpractice crisis here in Michigan simmered down a few years ago. Our then-governor, John Engler (a very conservative Republican) and the state legislature passed a fairly rigorous tort reform bill that greatly limited the ability of plaintiffs' attorneys to file suits. Among the other provisions were, first, that a prospective plaintiff had to submit a notice of "intent to sue" 18 months before the actual suit could be filed. The intent to sue had to have a signed statement from an "appropriate" physician stating that he/she agreed that the standard of care had been breached. An "appropriate" (that's my word, not in the law) physician was one *in the same specialty* as the prospective defendant, and the plaintiff's expert physicians had to be in the same specialty. A family practitioner, for example, can't testify against a neurosurgeon (although before this law, this sort of thing frequently occurred). Malpractice suits still take place in Michigan, but their numbers are greatly reduced.

Robert N. Frank, M.D. '66
Bloomfield Hills, Mich.

Access to appropriate care will be impeded

I work for a self-insured corporation, so the malpractice issue doesn't directly affect me. Our corporation does have a secondary insurer, and rates have gone up, but this hasn't yet translated into a change in my salary. The real change has come in the specialists to whom I refer patients. The vascular surgeon we use for complicated cases had trouble getting insurance this year because he does high-risk procedures. If he can't afford his insurance next year, my patients will get amputations instead of limb salvage. Some of my patients have lost their ob/gyns.

Richard Ihnat, M.D. '91
St. Louis, Mo.

Defensive medicine, the worst offense

The high cost of liability insurance is now in the limelight, but I believe there are two additional concerns which are actually of much greater importance. One is the enormous volume of "defensive medicine" and its detrimental effects on health care affordability. The other is the terrible loss of idealism among physicians and other health professionals, even if they themselves are never or seldom sued.

Hyman J. Milstein, M.D. '75
Studio City, Calif.

"We were all losers"

I am a local health director in West Haven, Conn., and our small malpractice insurance story is the following. We have had a semiretired urologist running our STD clinic for years. A few years back his insurance rates got doubled, and even if we certified that he was only doing this small amount of clinical public service work, they would not cut him a break. He ended up retiring rather than getting paid enough to cover his insurance premium. We lost a wonderful, gentle and experienced doctor, and he lost a major connection to feeling useful and vital in his life, albeit for only a few clinical hours per week. We were all losers in this, even the insurance company, which now no longer gets his premiums and never had to pay out for him for the 15 years he worked with us!

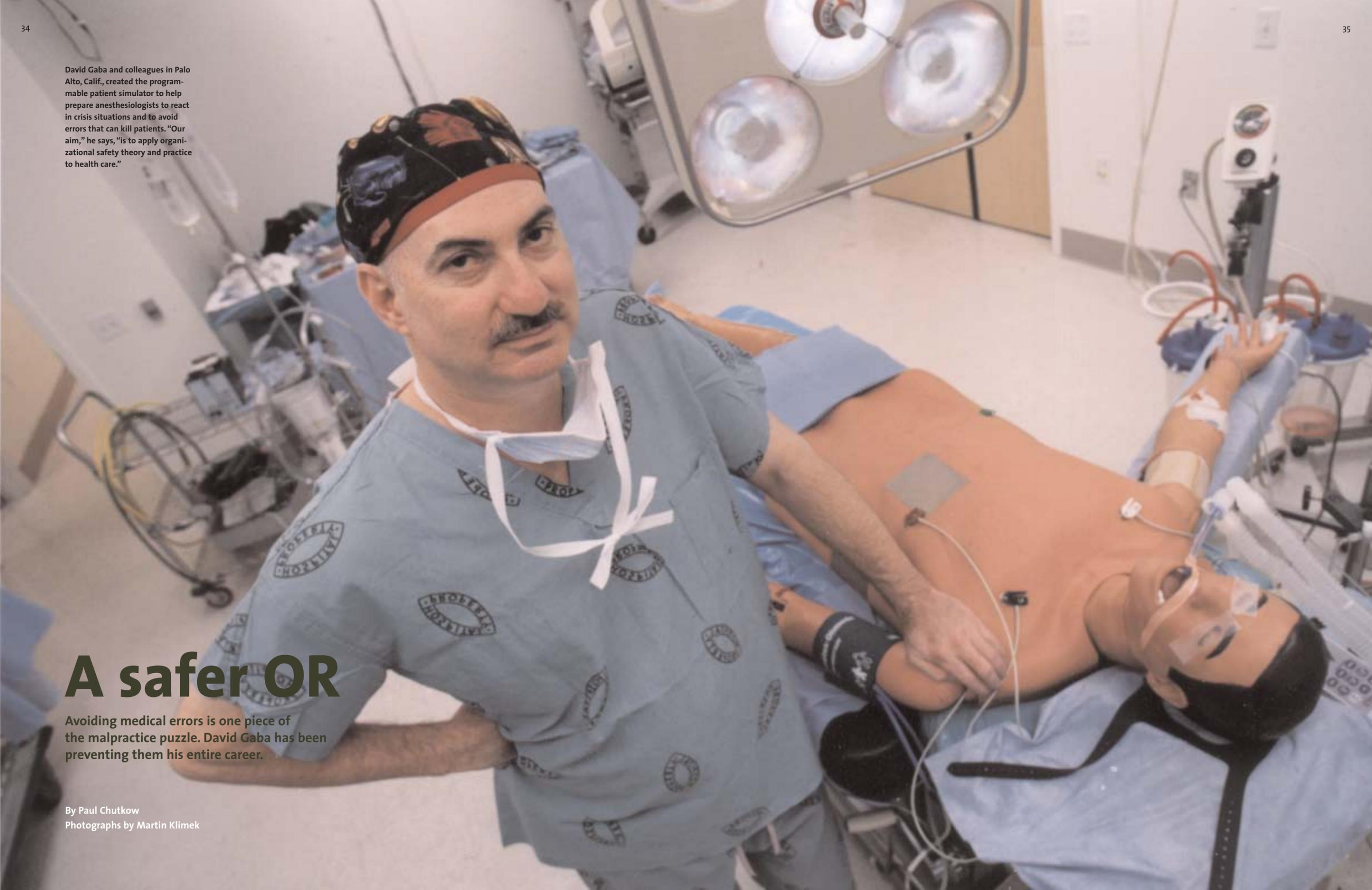
Eric Triffin, M.P.H. '86
Bethany, Conn.

David Gaba and colleagues in Palo Alto, Calif., created the programmable patient simulator to help prepare anesthesiologists to react in crisis situations and to avoid errors that can kill patients. "Our aim," he says, "is to apply organizational safety theory and practice to health care."

A safer OR

Avoiding medical errors is one piece of the malpractice puzzle. David Gaba has been preventing them his entire career.

By Paul Chutkow
Photographs by Martin Klimek



David M. Gaba, M.D. '80, was bent over the operating table, working intently on a car crash victim. The woman had suffered a broken leg, and Gaba and his surgical team were busy repairing the damage. For a time, everything went according to plan. Then, the team noticed climbing blood pressure and a dropping heart rate—an unusual combination that suggested a problem in the brain. One of the victim's pupils began to dilate.

"It's the left eye," said the attending anesthesiologist. "Looks like potential trauma to the head."

The anesthesiologist immediately called for back-up from a neurosurgeon, then moved into a set of carefully scripted emergency procedures. Hyperventilation, to reduce pressure inside the victim's brain. A steroid, to reduce inflammation and pressure. Then a diuretic to draw water from the brain. Despite these temporizing measures, a hole would probably have to be drilled in the victim's head to release the pressure.

As Gaba and his team worked, three video cameras monitored their every move and computers monitored the patient's electrocardiogram, blood pressure, blood oxygen saturation, carbon dioxide output and more. After

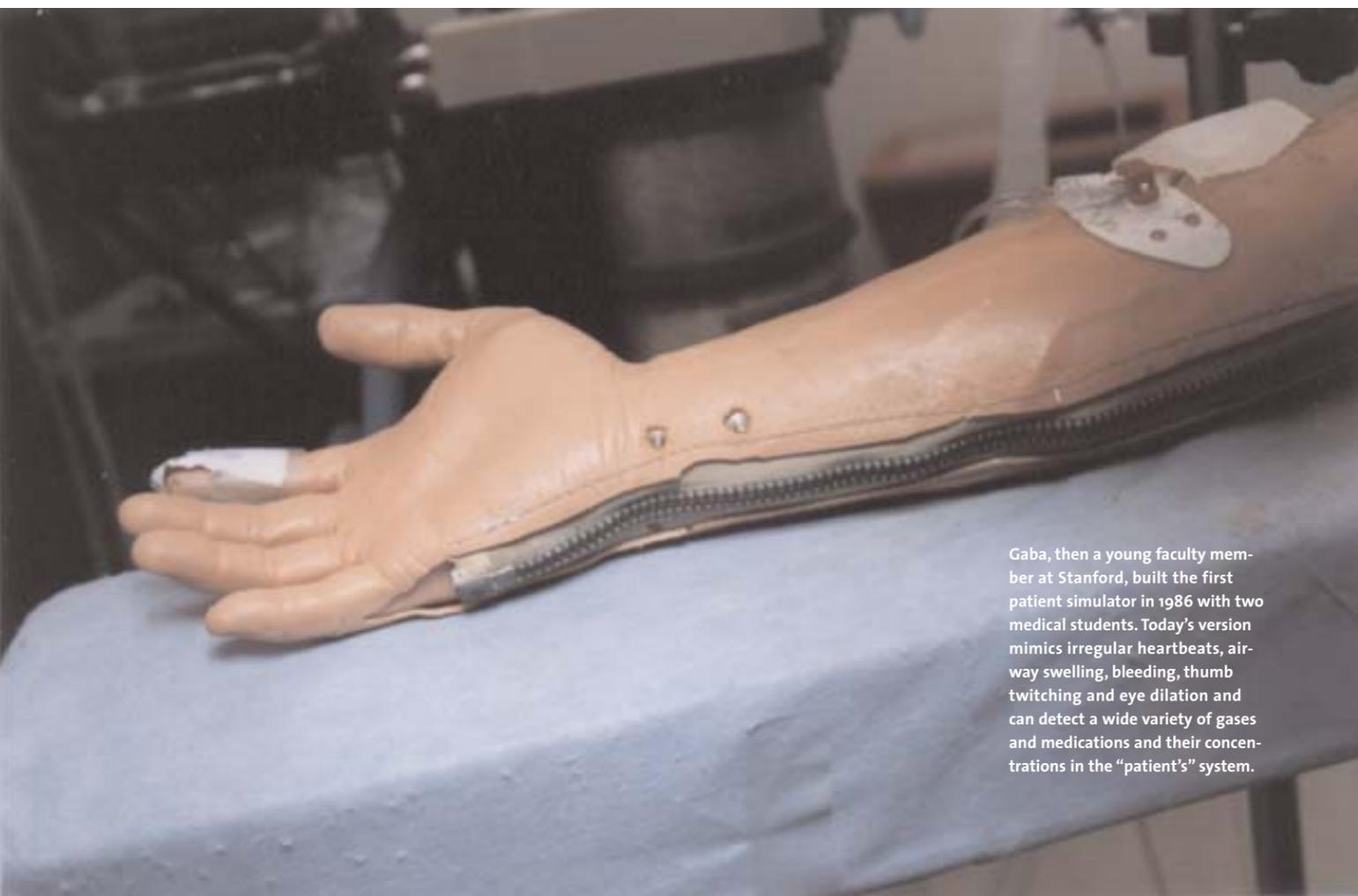
the surgery, Gaba and his team could go back through every stage of the crisis to see how they had performed—and where they could improve. In a few minutes, the crisis was over, but the patient did not exactly come through alive.

Why? This "patient" was actually a programmable polymer mannequin laced with wires and sensors—the centerpiece of an innovative crisis management training program that Gaba has developed with colleagues at the Veterans Affairs Palo Alto Health Care System and Stanford University School of Medicine. The aim of the program is to teach anesthesiology residents and more experienced practitioners how to respond in sudden and often unpredictable crises.

Training like an astronaut

"Most medical schools are very good at teaching normal medical procedures," Gaba explained. "The point of simulation training is to expose people to events and challenging situations they have not seen before, but could see, and then use them as generic springboards to teach all the behavioral issues of crisis management, dynamic decision-making, leadership and teamwork, and the processing of information. Those things have not been traditionally taught in health care."

Though he pretended to be a surgeon during today's simulation, Gaba is a veteran anesthesiologist with a passion



Gaba, then a young faculty member at Stanford, built the first patient simulator in 1986 with two medical students. Today's version mimics irregular heartbeats, airway swelling, bleeding, thumb twitching and eye dilation and can detect a wide variety of gases and medications and their concentrations in the "patient's" system.

for research and advanced simulation techniques. He serves as the director of the Patient Safety Center of Inquiry, which he created at the VA facility in Palo Alto, and as a tenured professor of anesthesiology at Stanford medical school. One day a week Gaba works clinically in the real OR, and the remainder of the week he conducts research or these kinds of training sessions. He and his colleagues have refined their simulation-based training course into an effective teaching tool that is now being adopted by other hospitals and universities here and abroad, including Harvard, Penn State, UCSF and Yale. The key is creating lifelike situations in dynamic clinical settings like the ER, the ICU and the OR, as with today's car-crash victim.

"We believe that part of a doctor's training should be comparable to that of a pilot or an astronaut. Doctors should know how to respond to medical crises—and to external crises such as equipment failures, power failures and even earthquakes." To support their training program, Gaba and his team have published a textbook on crisis management to improve human performance—and reduce mistakes—in the operating room. "Our aim," Gaba said, "is to apply organizational safety theory and practice to health care."

Thanks to this innovative work, Gaba is now widely regarded as an important pioneer in the field of medical

simulation and patient safety. In his book *Complications*, author Atul Gawande, M.D., M.P.H., credits Gaba among several figures in anesthesiology responsible for drastically cutting the rate of accidental deaths. Before reformers like Ellison C. Pierce Jr., M.D., and Jeffrey B. Cooper, Ph.D., pushed for systematic analysis of why anesthesia deaths occurred and instituted new practice standards, one or two patients died per 10,000 operations. Thanks in part to Gaba's anesthesia simulator, the number is now one in 200,000.

Gaba's contributions to medicine come as no surprise to his former mentors at Yale. "David was a superb medical student," recalled Roberta L. Hines, M.D., HS '77, professor and chair of anesthesiology at Yale. "He was always looking to do things in new and innovative ways." Hines said that Gaba's work has had a profound impact on Yale medicine and on the medical profession as a whole.

"Simulation has been a feature of NASA and the airline industry for many years, but David was certainly the first person to apply it to medicine in a rigorous way, using simulation for emergency procedures and the many repetitive things we do. At Yale, Hines said, "simulation has become an important part of the training process across the profession, not just for resident anesthesiologists but also for nurses, paramedics and emergency room personnel."

BELOW During the drill, a resident holds defibrillating paddles while another applies chest compression.



BOTTOM The action is observed from a control console and videotaped so that the participants can later analyze what they did right and wrong. Says Gaba: "We believe that part of a doctor's training should be comparable to that of a pilot or astronaut."



Despite his stature in the field, Gaba comes across not as an *éminence grise*, but as a spirited, overgrown technokid with some of the coolest toys on the block. In fact, much of the inspiration for his pioneering work traces right back to his childhood in Kansas City, Mo., and his early fascination with the NASA space program, which uses simulation for training and accident prevention. "I was one of those kids who audiotaped the TV broadcasts of all the Apollo missions," Gaba said. "And Alan Shepard's historic flight was launched on my seventh birthday."

Gaba attended Northwestern University, where he studied biomedical engineering and artificial intelligence, and he created for himself a specialized field of study called "high-level information processing." He entered Yale School of Medicine in 1976 and soon was doing research on defibrillators in the lab of Norman S. Talner, M.D., who at the time was chief of pediatric cardiology. "The hallmark of Yale for me, and I think for most people, was the freedom to learn the way we wanted to learn and investigate the things we wanted to investigate. I like the Yale System a lot and I benefited a lot from it."

After graduating in 1980, and after interning at the Yale-affiliated Waterbury Hospital nearby, Gaba moved to Stanford for a residency in anesthesiology. Soon after joining the faculty at Stanford, Gaba read a book that would set him on his path: *Normal Accidents*, by Charles B. Perrow, P.H.D., a professor emeritus of sociology at Yale. Perrow examined a series of accidents, including the nuclear disaster at Three Mile Island, and then analyzed the human, social and organizational errors that can lead to such accidents. Inspired, Gaba immediately decided to develop an accident-prevention program for the practice of anesthesia.

By 1986, Gaba and Abe DeAnda Jr., a medical student with a background in electrical engineering, were building their first "patient simulator." With John Williams, another medical student with an engineering background, they later created a more advanced simulator, whose successors Gaba and others continue to fine-tune today. Today's wondrous models, implemented on a single computer, can simulate an array of body movements and symptoms, including heart dysrhythmias, airway swelling, bleeding, thumb twitching, eye dilation and even the presence of a fetus. They can also detect a wide variety of gases and medications and their concentrations in the "patient's" system.

"We don't just do drills," Gaba said. "We try to replicate, as closely as we can and in a very high-level way, a real clinical environment. We focus on issues that we always expect people to be good at, but that nobody ever teaches us."

His childhood heroes at NASA would surely be impressed. **YM**

Paul Chutkow is a writer in Corte Madera, Calif.

BOB HAMBLBY



Knowing when it's time to quit

Still able at age 70, a physician contemplates his profession and his approaching irrelevance.

"My second fixed idea is the uselessness of men over the age of sixty."

—William Osler, 1905

Osler spoke those words in his last address at Johns Hopkins before he left to become Regius Professor at Oxford. He then went on to cite Trollope's novel *The Fixed Period*, in which an idea is advanced that men should retire at 60, spend a year in contemplation and then be chloroformed. Newspapers of the time missed Osler's jesting tone and took him seriously. A great brouhaha ensued, which caused Osler both considerable distress and some amusement.

To read Osler today is to experience some of the best aspects of humane and medical thought of the Victorian era. Much of that thought is not outmoded.

I retired in 2000. When I told people what I planned, they asked why. I was 67, apparently fit, enjoyed an interesting practice and my mind seemed not to be failing. Of course, there were and are lots of good reasons to leave practice: HMO intrusiveness, decreasing reimbursement, loss of collegiality in medical communities

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and suchlike. But these matters were not really at the root of my decision.

When they get to a certain age, doctors should retire. As they age, they become increasingly irrelevant to their medical communities. The generational difference that slowly develops makes communication less cordial. True, we all belong to the same fraternity, but the handshake changes. Doctors are usually happiest when they confer and refer within an age radius of 10 or 15 years. The tone of a medical community is usually set by doctors in their 40s and early 50s. I practiced in one community for over 30 years. Doctors who stood at the pinnacle of the profession when I arrived slowly became "Dr. Who?"

Usually they did not know that their knowledge was slipping. They probably did not know it because their loyal patients continued to love them. It was sad to see. I did not want it to happen to me. I could see it would have happened. There were many doctors in our area and some in my group who were younger than my children. Many of them could not bring themselves to call me by my first name. I gradually lost the intense desire to know everything in my field, and even if I had kept the desire, it would have been impossible to do so.

In order to use new knowledge one must have a schema, a sort of intellectual hat rack, on which to hang new concepts. I did not have an up-to-date intellectual schema to incorporate what I understand of genetics and molecular biology. Even many of the titles, much less the contents, of articles in my specialty journals were incomprehensible to me. It is in these new fields

that basic knowledge is growing, and clinicians should have a grasp of their specialty's basic science. And, as far as clinical information goes, in my field of gastroenterology, much of it seemed to me to be recycled knowledge arrived at by newer methods. It may have come with better statistics or larger patient populations or with MRI and endosonography instead of barium and fiber optics, but it did not help an experienced physician take better care of his patients. At major meetings I increasingly found myself choosing between papers I had no background to understand and symposia that told me little, as I watched hordes of young men and women bustle past.

Medicine is a unique activity. It offers the opportunity to engage simultaneously in intellectual problem solving, humane ministering and, in some areas, technical expertise. I retired after 34 years of practice, 45 years after entering medical school—really, more than a generation ago. It has been a time of tremendous, awesome, unforeseen developments in medicine and I had a wonderfully satisfying career. I think what Osler had in mind when he gave *The Fixed Period* address was the relationship of physicians to their colleagues and to new knowledge. Doctors should not be chloroformed but they should retire.

Herbert J. Kaufmann, M.D. '59, is a retired gastroenterologist in Bedford, N.Y. Since leaving medicine three years ago, he has devoted himself to family activities, stained-glass making, genealogy and, he says, "being on vacation."

Psychologist to lead Graduate School

As dean, Peter Salovey hopes to bridge a gap that is cultural as well as geographic.

"There's probably no farther walk on this campus than from the Sterling Hall of Medicine to the Kline Biology Tower," says psychologist **Peter Salovey**, PH.D. '86, the new dean of the Graduate School of Arts and Sciences. For graduate students on the medical campus, isolated from fellow students in other fields, says Salovey, "this is more than just a geographical problem: it is a cultural problem."

In his new role as dean of the 760 faculty members and 2,300 students in the arts and sciences—that is, all students at Yale working toward M.A., M.S. and PH.D. degrees—Salovey hopes to bridge that divide and bring together graduate students separated by discipline as well as geography. He will rely to a large degree on the McDougal Graduate Student Center, located at the Hall of Graduate Studies on York Street about halfway between Sterling and Kline, which offers career counseling, seminars in teaching, social events and a place simply to hang out. Salovey hopes that graduate students will be increasingly likely to trek over from the medical campus to take part in the McDougal Center's activities, and also will encourage the center to offer programs on Cedar Street.

Salovey foresees an expanded role for the McDougal Center as a sponsor of public service programs, which already offer opportunities for graduate students to meet one another and to



Peter Salovey

get involved in the larger New Haven community. "We're very interested in encouraging community volunteerism and participation in social policy and social concerns," Salovey said. "I will be working closely with the McDougal Center fellows who already are organizing such community service experiences."

Salovey succeeds neuroanatomist Susan Hockfield, PH.D., who in January became the first scientist appointed provost of the university. As did Hockfield, Salovey plans to keep his laboratory running, spending Fridays there. Salovey does basic research into how human emotions influence thought and action. With colleague John D. Mayer, PH.D., he developed the notion of "emotional intelligence," the view that just as people have a wide range of intellectual abilities, they also have a repertoire of measurable emotional skills and competencies that profoundly affect their functioning. As deputy director of the Center for Interdisciplinary Research on AIDS, he investigates the effectiveness of health promotion messages in persuading people to change risky behaviors, and he has conducted similar work on health communications targeting cancer prevention behaviors. In a quasi-academic role, Salovey also plays stand-up bass for the Professors of Bluegrass.

—Cathy Shufro

NOTES

Robert L. Bell, M.D., an assistant professor of surgery (gastroenterology) who specializes in minimally invasive and bariatric surgery, performed the first laparoscopic gastric bypass at Yale in August 2002, a month after joining the faculty. Interest in gastric bypass surgery, a technique he learned as a fellow at the University of Maryland, is on the increase after last year's Dateline NBC broadcast on weatherman Al Roker's successful procedure.

The Yale Medical Group recently announced the following appointments: **James A. Brink**, M.D., professor of diagnostic radiology, has been named interim chair of diagnostic radiology. Brink, who also holds a degree in electrical engineering, was elected to membership in the Society of Computed Body Tomography and Magnetic Resonance and has twice been a recipient of the Godfrey Hounsfield Award for Research Excellence in Computed Tomography. **Anne McB. Curtis**, M.D. '70, HS '75, professor of diagnostic radiology, will serve as vice chair of clinical affairs and oversee the clinical quality improvement initiative. **Vladimir Neklesa**, M.D., associate research scientist in diagnostic radiology, will continue as director of information technology and partner with Yale-New Haven Hospital to further implement the Picture Archive and Communication System, which enables e-delivery of images to referring physicians for rapid interpretation. **Howard P. Forman**, M.D., associate professor of diagnostic radiology, who continues as vice chair for finance and administration, will assist in evaluation of all outpatient opportunities.

José Costa, M.D., deputy director of the Yale Cancer Center and professor and vice chair of pathology, was awarded the Josep Trueta Medal by the Catalan government in Barcelona in February. The medal recognizes

scientists who have had a profound impact on the scientific community in Catalonia. Costa, who is the principal investigator of the Marcia Israel Laboratory for the Earlier Detection of Breast Cancer at Yale, focuses his research on carcinogenesis and tumor progression.

Michael H. Ebert, M.D., former chair of psychiatry at Vanderbilt University School of Medicine, was appointed professor of psychiatry at Yale, chief of staff of the VA Connecticut Healthcare System and associate dean for veterans affairs at the School of Medicine last fall. Ebert's focus has been in clinical pharmacology. He directed a clinical research program in the section of experimental therapeutics, part of the intramural program of the National Institute of Mental Health. Ebert serves as director of the American Board of Psychiatry and Neurology (ABPN) and is director of the Psychiatry Council and vice president of the ABPN. He also serves on the residency review committee for psychiatry of the Accreditation Council on Graduate Medical Education and occupies a seat on the American Board of Medical Specialties. Ebert was recently elected to the executive council of the Association of American Medical Colleges and is a representative to the Council of Academic Societies.

Jack A. Elias, M.D., the Waldemar Von Zedtwitz Professor of Medicine, received the Recognition Award for Scientific Accomplishment from the American Thoracic Society in May. The award is given to individuals for distinguished scientific contributions to the understanding, prevention and treatment of lung disease.

Charles A. Greer, PH.D., professor of neurosurgery and neurobiology and co-director of the Interdepartmental Neuroscience Program, has received the 2002 Frank Allison Linville's R.H.

Wright Award in Olfactory Research. Greer visited Simon Fraser University in Vancouver and the University of British Columbia in the spring to receive the \$30,000 annual award and deliver lectures and research seminars. He was honored for his studies of the fine structure and function of the developing olfactory system, especially local synaptic circuit organization in the olfactory bulb. These studies use the olfactory system as a model for identifying mechanisms and general principles that underlie the specificity of axon targeting and synapse formation in the nervous system.

Sharon K. Inouye, M.D., M.P.H. '89, professor of medicine (geriatrics) and associate clinical professor of nursing, received the 2003 Ewald W. Busse Research Award in the Biomedical Sciences during the 3rd Pan-American Congress of Gerontology in April in Buenos Aires. The award recognizes achievements of promising junior or midcareer scientists and is intended to encourage their continued contributions to aging research.

David L. Katz, M.D., M.P.H. '93, associate clinical professor of health policy and administration in epidemiology and public health and director of the Yale-Griffin Prevention Research Center, began writing a column on preventive medicine for Oprah Winfrey's magazine, *O*, in March after the magazine's editor heard him speak at an American College of Preventive Medicine meeting. Katz also writes a weekly column for the *New Haven Register*.

Donald R. Lannin, M.D., former director of the Leo W. Jenkins Cancer Center at North Carolina's East Carolina University (ECU), has joined the Yale faculty as professor of surgery (oncology) and executive director and co-medical director of the Yale Comprehensive Breast Center.

While at ECU, Lannin developed a comprehensive breast center program. He arrived at Yale last summer.

Sherwin B. Nuland, M.D. '55, HS '61, clinical professor of surgery (gastroenterology), received the John P. McGovern Medal from the American Medical Writers Association for pre-eminence in medical writing. The award was presented at the group's annual conference in San Diego in October. Nuland also received the McGovern Medal in 2001 from the University of Texas in Galveston and in 1995 from the American Osler Society.

M. Bruce Shields, M.D., Marvin Sears Professor of Ophthalmology and Visual Science and chair of ophthalmology and visual science, was named chair of the American Board of Ophthalmology (ABO) in January for a one-year term. Shields, certified by the ABO in 1975, served as an associate examiner from 1987 through 1995 and also on the board. In the capacity of an associate examiner he interviewed prospective diplomates in the oral examination process.

An item in the Faculty Notes section of our spring issue incorrectly referred to Nancy H. Ruddle, PH.D. '68, as an associate professor before her appointment as the John Rodman Paul Professor of Epidemiology and Public Health. Her previous appointment was professor. We regret the error.

SEND FACULTY NEWS TO Claire Bessinger, *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612, or via e-mail to claire.bessinger@yale.edu



Robert Bell



James Brink



Anne Curtis



Vladimir Neklesa



Howard Forman



José Costa



Michael Ebert



Jack Elias



Charles Greer



Sharon Inouye



David Katz



Donald Lannin



Bruce Shields

The crescendo of four years

On Match Day, the mood reflects a stellar list of residency placements, “by far the best we’ve ever had.”

In a scene that combined the envelope-opening excitement of the Academy Awards with the destination-determining drama of the NFL draft, more than 90 fourth-year medical students gathered at Marigolds on March 20 for Match Day, the annual ritual that decides where students will start their careers.

“I’m not too stressed, but I’m very, very interested to find out where I’ll be spending the next three or four years of my life,” said Gabe Simon. (His equanimity paid off as he got into his first choice, the emergency medicine program at the University Health Center of Pittsburgh.)

Marta Rivera said Match Day was even more stressful than the day she was accepted to medical school because “it affects more than just you. Other people are involved as well.” In Rivera’s case, her parents, her fiancé and his parents all hoped she’d match to an internal medicine residency at New York Presbyterian Hospital-Cornell because it is near the home of her future in-laws. (She, too, had her wish granted.)

Surveying the cafeteria, which was rapidly filling with students clutching cameras, bouquets and cell phones, Rivera said, “It’s nice to be able to share this with so many people going through the exact same thing at the exact same time.”

The scene at Yale was replicated around the country as more than

14,000 U.S. medical school seniors learned which residency programs they will be entering. The National Resident Matching Program was established in 1952 to create a mechanism for filling residency slots and promote fairness in the selection process. Applicants list their program preferences, program directors indicate their choice of applicants and a computer makes the matches. This year marked a record high in the number of applicants (23,965, including international medical graduates) and an all-time high in the number of residency positions offered—23,365, up 450 from last year. A record 575 couples participated in the Match as partners.

At the stroke of noon students shouted and clapped as they pushed toward the door of the dining hall like fans at a rock concert. Nimi Tuamokumo tore open her envelope with shaking hands. Then she let out a loud scream and fell to her knees in tears—she’d been accepted into her first choice, Brigham and Women’s Hospital’s radiation oncology program.

“It’s weird. This is all I’ve been talking about for the last four months,” said Andrew Cooper, who was pleased to learn he’ll be specializing in orthopaedic surgery at Jackson Memorial Hospital

in Miami. “I don’t know what I’m going to talk about now.”

Richard Breck, M.D. ’45, who was among several alumni on hand for a Match Day luncheon, said the emotional intensity of the scene in Marigolds was far different from when he was a medical student in the days before the match. “This is far more alive,” he said, gesturing toward several students in a group hug. “Of course the war was still on, so that was a factor, but my memory is that one by one we went to our mailboxes and opened our envelopes alone.”

When the 2003 Match concluded, 94 Yale medical students knew what the next big step in their career paths would be. Nancy R. Angoff, M.P.H. ’81, M.D. ’90, HS ’93, associate dean for student affairs, said dermatology (always a draw at Yale because of the strength of the program) and radiation oncology were popular fields among students this year, with five and four placements, respectively.

“Students think of them as lifestyle fields,” she said. “They don’t have a lot of emergencies, so their lives are a little more predictable.” A regular schedule also makes these fields more amenable to dual careers in clinical medicine and research, Angoff said.



TERRY DAGRADI (2)

The salaries also tend to be higher, which is important to students, who leave Yale carrying an average debt of \$100,000.

Based on the “overall sense of happiness” in Harkness Lounge and the quality of the programs the students got into, Angoff called the 2003 Match “by far the best we’ve ever had.” She credits the current class of graduates as well as Yale alumni. “If they weren’t doing well in their residencies, the hospitals wouldn’t want our current students,” she said.

—Jennifer Kaylin



ABOVE With a cell phone and a bouquet, Nimi Tuamokumo, left, and Roselia Guillen-Santana celebrated their matches.

LEFT Pamina Kim gets a hug from Katherine Gergen as they share the news of Kim’s match.

2003 residency placements for Yale medical students

The Office of Student Affairs has provided the following list, which outlines the results of the National Resident Matching Program for Yale’s medical graduates. Some names appear twice because the graduate is entering a one-year program before beginning a specialty residency. The transitional designation is a one-year program with three-month rotations in different specialties.

California

Loma Linda University
Michael Bolton, plastic surgery

Santa Clara Valley Medical Center, San Jose
Warren Kim, transitional

Stanford University Programs
Jennifer Chao, medicine-preliminary
Dita Gratzinger, pathology
Richard Hsu, general surgery
Daniel Pham, diagnostic radiology

UCLA Medical Center
Ryan Barton, anesthesiology

UCLA–VA Greater Los Angeles Healthcare System
Charlton Kim, internal medicine

University of California, San Francisco
Adrian Hinman, orthopaedic surgery
Pamina Kim, internal medicine
Warren Kim, diagnostic radiology
David Lao, internal medicine
Saeher Muzaffar, internal medicine

University of Southern California, Los Angeles
Jennifer Chao, ophthalmology

Canada

McGill University, Montreal
Matthew Stiebel, orthopaedic surgery

Connecticut

Greenwich Hospital
Kevin Johnson, medicine-preliminary

Hospital of Saint Raphael, New Haven
Jennie Bailey, transitional

Yale-New Haven Hospital

Leah Ahoya, obstetrics and gynecology
Justin Cohen, surgery-preliminary, urology
Charles Dela Cruz, internal medicine
Michael DiLuna, surgery-preliminary, neurosurgery
Daniel Kanada, medicine-preliminary, diagnostic radiology
Maxwell Laurans, surgery-preliminary, neurosurgery
Ryan Lieberman, psychiatry
J. Ryan Martin, obstetrics and gynecology
Jennifer Nam, dermatology

Melissa Pradhan, internal medicine/primary
Jeffrey Seiden, pediatrics
Christopher Severson, medicine-preliminary
Elaine Shay, ophthalmology
Abhishek Sinha, internal medicine
Joahd Toure, internal medicine
Juan Vasquez, surgery

Delaware

Christiana Care, Wilmington
Elaine Shay, medicine-preliminary

District of Columbia

Georgetown University Hospital
Ryan Barton, transitional

Florida

Jackson Memorial Hospital, Miami
Andrew Cooper, orthopaedic surgery

Indiana

Indiana University School of Medicine, Indianapolis
Caron Farrell, pediatrics/psychiatry/child psychiatry

Iowa

University of Iowa Hospitals and Clinics Program, Iowa City
Todd Fairchild, orthopaedic surgery

Maryland

Johns Hopkins Hospital, Baltimore
Mathew Augustine, general surgery
Justin Bekelman, medicine-preliminary
Scott Berkowitz, internal medicine
John Koo, ophthalmology
Amar Krishnaswamy, internal medicine
Maya Lodish, pediatrics
Jennifer Teitelbaum, psychiatry

University of Maryland Medical Center, Baltimore

Jennifer Teitelbaum, medicine-preliminary

Massachusetts

Beth Israel Deaconess Medical Center, Boston
David Geist, medicine-preliminary
John Koo, medicine-preliminary

Boston University Medical Center
David Geist, dermatology
Anil Shivaram, ophthalmology

Brigham and Women’s Hospital, Boston
Adam Cuker, internal medicine
Namita Kumar, internal medicine/primary
Vivek Murthy, internal medicine/primary
Abhijit Patel, radiation oncology
Jennifer Schutzman, internal medicine
Nimi Tuamokumo, radiation oncology

Brigham/Faulkner Hospital, Boston

Jennifer Nam, medicine-preliminary

Children's Hospital of Boston

Patricia Diaz, pediatrics

Roselia Guillen-Santana,

pediatrics/primary

Lisa Roy, pediatrics

Harvard Combined Program, Boston

Margaret Bourdeaux, medicine/

pediatrics

Gregory DeBlasi, orthopaedic surgery

Lahey Clinic Program, Burlington

Micah Jacobs, surgery-

preliminary, urology

Massachusetts General Hospital, Boston

Essmaeel Abdel-Dayem, diagnostic

radiology

Wael Asaad, surgery-preliminary,

neurosurgery

Tracey Cho, medicine-preliminary

Christopher Cutie, surgery-

preliminary, urology

Abigail Donovan, pediatrics-

preliminary, psychiatry-

adult and child

Karin Finberg, clinical pathology

Massachusetts General**Hospital/Brigham and Women's****Hospital, Boston**

Tracey Cho, neurology

Christopher Severson, neurology

Mount Auburn Hospital, Cambridge

Anil Shivaram, medicine-preliminary

Nimi Tuamokumo, medicine-

preliminary

Tufts University, Malden

Rebecca Seekamp, family practice

Michigan**University of Michigan Hospitals,****Ann Arbor**

Colin Greineder, emergency medicine

Daniel Mayman, psychiatry

Minnesota**Hennepin County Medical Center,****Minneapolis**

Jianling Yuan, transitional

University of Minnesota Medical**School, Minneapolis**

Jianling Yuan, radiation oncology

Missouri**Barnes-Jewish Hospital, St. Louis**

Kevin Johnson, diagnostic radiology

Rahel Nardos, obstetrics and

gynecology

New Hampshire**Dartmouth-Hitchcock Medical****Center, Lebanon**

Clare Drebitko, pediatrics

Khashayar Farsad, surgery-

preliminary, neurosurgery

New York**Long Island Jewish Medical Center,****New Hyde Park**

Michael Tang, emergency medicine

Memorial Sloan-Kettering Cancer**Center**

Justin Bekelman, radiation oncology

Abhijit Patel, transitional

Mount Sinai Hospital

Jason Baynes, orthopaedic surgery

Lysiane Ribeiro, psychiatry

Arien Smith, surgery-

preliminary, neurosurgery

Mount Sinai School of**Medicine-Cabrini**

Daniel Pham, medicine-preliminary

Daniel Saketkhoo,

medicine-preliminary

New York Presbyterian**Hospital-Columbia**

Saeed Ahmed, pediatrics

Kathryn Teel, pediatrics

New York Presbyterian**Hospital-Cornell**

Jennie Bailey, dermatology

Mary-Ann Etiebet, internal

medicine/primary

Marta Rivera, internal medicine/

primary

New York University School**of Medicine**

Essmaeel Abdel-Dayem, medicine-

preliminary

Boris Veysman, emergency medicine

Queens Hospital/Mount Sinai

Michael Tang, medicine-preliminary

North Carolina**University of North Carolina****Hospital, Chapel Hill**

Matthew Goldenberg, general

psychiatry

Ohio**Cleveland Clinic Foundation**

Louie Enriquez, medicine-preliminary,

diagnostic radiology

Anya Mari Szeplin, medicine-

preliminary, dermatology

Pennsylvania**Hospital of the University of****Pennsylvania, Philadelphia**

Steven Farmer, internal medicine

Satish Nagula, internal medicine

Daniel Saketkhoo, diagnostic radiology

Grace Suh, internal medicine

University Health Center**of Pittsburgh**

Gabriel Simon, emergency medicine

Rhode Island**Rhode Island Hospital/Brown****University, Providence**

Mari Rebane, general surgery

Utah**University of Utah Affiliated****Hospitals, Salt Lake City**

Daniel Kline, medicine-preliminary,

ophthalmology

Washington**Madigan Army Medical Center,****Tacoma**

Garth S. Herbert, general surgery

University of Washington Affiliated**Hospitals, Seattle**

John Cowden, pediatrics

Matthew Kronman, pediatrics

Michael Gregory Thompson, pediatrics

Bertrand Wicholas, psychiatry

Wisconsin**Medical College of Wisconsin****Affiliated Hospitals, Milwaukee**

Melissa Chiang, medicine-

preliminary, dermatology

Younghoon Cho, plastic surgery



TERRY DAGRADI

Christopher Severson and Patricia Diaz were among the first to enter the lounge to get their match letters.

Still smokin', still addictive

A sizzling second-year show spins the tale of a “healthy” cigarette and a fiendish plot to steal its formula.

Ever since his arrival at Yale in 1997 fresh from his battles with the tobacco industry as head of the Food and Drug Administration, Dean David A. Kessler, M.D., has provided fodder for the second-year show. In 1998 students teased him with a song called “FDA Dropout.” Another recent show featured a video of Kessler sneaking out of a bathroom to the tune of “Smokin’ in the Boys’ Room.”

Kessler has encouraged this tradition by “buying” his way into the show each year with a donation to local charities. Included in his annual largesse are roles for Nancy R. Angoff, M.P.H. ’81, M.D. ’90, HS ’93, associate dean for student affairs, and Ruth J. Katz, J.D., M.P.H., associate dean for administration.

This year Kessler portrayed himself and paid lip service to the virtues of a vegetarian, low-sodium, lactose-free “healthy cigarette” developed at Yale. Then Kessler, the author of a “well-written but soporific” book on the tobacco industry, helped steal the sole copy of the cigarette’s formula. Had Big Tobacco finally bought him off?

So it seemed until two secret agents traced the theft to Dr. Evil, transplanted from the set of an Austin Powers movie to join the Class of ’05—make that ’005—in “The Spy Who Smoked Me.” The healthy cigarettes, tested at Yale in a randomized, quadruple-blind, double-deaf, one-third-mute study,

1) Where would James Bond be without a scene in a casino? The second act of “The Spy Who Smoked Me” opened with a tap dance routine set during Casino Night.

2) When an urgent assignment pulled Gold Bond, played by Doug Walled, away from a tryst with Carrie Sokol, she consoled herself by singing “The Beeper Is Forever.”

3) Bond Girl Mihae Yun, in dark glasses, played the lethal Agent XX, who danced through “I’m Your Worst Nightmare/Voulez-Vous Kung Fu Avec Moi.”

4) The show closed with the gathering of the Class of 2005 on stage to sing “We’ve Got Yale Med/Who Could Ask for Anything More?”



1

were still addictive, as revealed in a disco dance-off as Kessler and Angoff struggled for the last butt. With the two deans in the grip of Saturday Night fever, Katz (“I bought my way into the show”) filched the last cigarette in the administrators’ stash.

To the rescue came Gold Bond (Douglas Walled) and Agent XX (Mihae Yun), the lithe and chromosomally correct brains behind the investigation, who recovered the formula.

The show netted almost \$6,000 for the Boys and Girls Club of New Haven.

—Cathy Shufro



2



3



4

Back to school with Colombia's top doctor

José Patiño, an old hand in Latin American medicine and education, has a new use for the Yale System.

By John Curtis

Although he believes that Colombia already has too many medical schools, José Félix Patiño, M.D. '52, HS '58, is leading a drive to create one more. He hopes the new school—a joint venture of the prestigious Universidad de Los Andes and the Fundación Santa Fe de Bogotá (FSFB), a medical center Patiño and others founded 20 years ago thanks to the philanthropic gift and dedication of Alfonso Esguerra, M.D. '64, and his wife, Gloria—will raise the level of medical education in Colombia. Patiño's model for the new school is the Yale System of medical education.

"The main thing that we are taking from the Yale System is the flexibility of the curriculum and the responsibility the student has in learning, and not only what the teacher provides the student. The students have to learn how to learn and be students for the rest of their lives," Patiño said in January during a telephone interview from his home in Bogotá, Colombia's capital. "When I was a medical student at Yale, my fourth year was practically ad-libbed. I could do whatever I wanted because I had completed all my subjects, and that gave me the opportunity to attend lectures and classes in other subjects all over the university."

This new medical school, scheduled to open next year, will be the latest in a string of achievements in medicine, education and social welfare that Patiño has brought to his nation during a 45-year career. Since returning home after his education and training in surgery at Yale, Patiño has served Colombia as director of the Association of Medical Colleges, minister of health, rector of the National University and president of the National Academy of Medicine. He worked with John D. Rockefeller III and Robert S. McNamara to bring Rockefeller Foundation and World Bank grants to Colombia. In recent years he also found time to write a biography of the opera diva Maria Callas.

As minister of health in the mid-1960s, Patiño introduced generic drugs to Colombia, dramatically lower-

ing the cost of medications. While rector of the National University, one of the country's largest public colleges, Patiño restructured 34 distinct faculties, brought in full-time faculty and obtained funding for teachers and researchers.

Patiño has continued to indulge his passion for opera, acquired from his father, also a physician, who took his family to listen to operas at Bogotá's Teatro Colón. While at Yale, Patiño traveled to New York to hear a new singer with a marvelous voice who, although well-known in Europe and Latin America, had yet to make her debut in the United States. That singer was Maria Callas. "I became interested in her life, always in search of perfection," says Patiño. "I own every opera she recorded but three. She sang operas that had been in obscurity and brought them to light." Two years ago Patiño's biography of Callas, now in its second edition, was published by Editorial Kimpres of Bogotá. He is the author of 18 monographs, over 300 papers and eight books, including a major surgery textbook dedicated to his professor at Yale, the late Gustaf E. Lindskog, M.D. This fall he will deliver the Distinguished Lecture of the International Society of Surgery (of which he was president) at the annual Clinical Congress of the American College of Surgeons in Chicago.

Looking back on the heady days of the 1960s, when he hobnobbed with McNamara and Rockefeller and served on a delegation that welcomed President John F. Kennedy on a state visit to Colombia, Patiño laments a change in international lending practices. "At that time the World Bank had a different philosophy than it has today. Their philosophy was that of John F. Kennedy, to help the poor," he says. "To see how the World Bank functions today, pushing globalization without considering the local situation, is traumatic."

The Fundación's vision of helping the poor has become reality in six low-income neighborhoods bordering its teaching hospital. The 180-bed hospital and medical center was the first in Latin America to have its own full-time staff of physicians. (Typically, Patiño says, hospitals in Latin America rely on the services of physicians who work part time while maintaining private practices.) Its mission includes the education and training of physicians, as well as providing medical care. Proceeds from the center's clinical fees subsidize services for the poor that go

Since graduating from medical school, José Patiño has served as Colombia's minister of health, led a reform of the National University there and written a biography of Maria Callas. Now he is leading an effort to create a new medical school modeled on the Yale System.



TERRY DAGRANDI

beyond health and medicine. "The community health program is not only a health program," Patiño says. "It not only relates to outpatient centers, but also to community development in terms of the environment and starting people on their own small industries. It has been a tremendously effective community program."

Several members of the Yale medical faculty have traveled to Colombia to see the foundation and its programs firsthand. Among them are former Dean Gerard N. Burrow, M.D. '58, HS '66; former Deputy Dean Robert H. Gifford, M.D., HS '67; Yale-New Haven Hospital President Joseph A. Zaccagnino, M.P.H. '70; and former Chief of Staff John E. Fenn, M.D. '61, HS '66 (to whom Patiño refers as his brother).

The center also brought medical students from the United States to Colombia for training periods of two months to a year. During the 1990s, several came from Yale to a hospital in a small town outside Bogotá. Concerns over security put an end to that program, however.

Patiño's desire to attack poverty comes from a long-held belief that it lies at the root of Colombia's troubles. Two left-wing guerrilla groups who claim to speak for the downtrodden are at war with both the government and right-wing paramilitary groups. Both the paramilitaries and

the guerrillas fund their activities through alliances with drug traffickers.

"The political system here is really complicated," says Patiño. "The principal reason is the poverty, the extreme difference between the people of the higher socioeconomic class and the people in the lower level. There is a tremendous disparity and it is increasing instead of decreasing."

Despite the prevailing image of Colombia as a country torn by warfare and strife, with large swaths of land under the control of guerrillas or paramilitaries, Patiño says Bogotá is a safe place. "If you come to Bogotá today you will find a normal city; entertainment, movies, restaurants," he says. Also, he adds, Colombia is a marvelous country that has produced figures of the stature of Nobel laureate Gabriel García Márquez, painter Fernando Botero, rock artist Shakira and Formula One racer Juan Pablo Montoya.

He is optimistic that the country's recently elected president, Alvaro Uribe, who campaigned on a slogan of a "firm hand" with insurgents, can improve the political situation. In the meantime, life goes on and he continues with his plans for the new medical school.

The new school, Patiño says, should be up and running by January 2004. Why would someone who believes there are too many medical schools want to add one more? In the 1970s, there were only eight in this country of 41 million people. Now there are 45, most of which were established in the past decade since the national government began to promote higher education by encouraging the opening of new universities. "Many of them are really of very poor quality," Patiño says of these schools. "The great contribution we think we will make is to set higher standards in medical education and serve as a model for other medical schools in Colombia and Latin America."

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

In *Lost in America*, a Yale surgeon opens up memories of his father

The latest and most personal book by **Sherwin B. Nuland**, M.D. '55, HS '61, *Lost in America: A Journey With My Father*, grew first and foremost out of his need to dissect his tangled feelings of love and resentment toward his immigrant father. But Nuland's memoir about his impoverished childhood in the Bronx also arose from his discomfort about how others view him today: those who have known Nuland as the urbane surgeon, scholar and internationally known writer have seen a public face whose polish reveals nothing of "the long road to get there."

Nuland opens his book with an epigraph: "Be kind, for everyone you meet is fighting a great battle." The book tells not only the story of his father's tragedies but also the story of Nuland's own "great battle"—his struggles with death, depression, anti-Semitism and shame.

"For many people who haven't spent a lot of time with me," says Nuland, a clinical professor of surgery at Yale, "I was some kind of a cool WASPY guy who comes from a very American background and has things all figured out. ... But I'm also this other complex, confused person. The whole idea is that each of us is a bundle of inconsistencies."

Some of Nuland's confusion stems from growing up with a father who devoted himself to his wife and children but who raged against them, frustrated by his own failures and misfortunes. Nuland's nagging awareness that he needed to examine his feelings about his father remained in "the back pocket" of his mind for several years after the 1994 publication of *How We Die: Reflections on Life's Final Chapter*. The book was tremendously successful, winning the National Book Award and selling a half-million copies in the United States alone. But readers pointed out something that shocked Nuland: he had inti-

mately described the illnesses of several family members without once mentioning his father.

"I didn't understand why I'd left him out of the book," says the 72-year-old Nuland in a late-winter interview in the office of his colonial house in Hamden, Conn. He realized, "I'm never going to really understand him until I write about him."

Nuland begins his story not with an account of his father but with a scene from his own nightmarish year in a mental hospital when, at age 42, he was suffering from severe depression. The dispirited Nuland adopted the stooped posture and helplessness of his father, 15 years dead.

That father was an immigrant from Bessarabia, then claimed by Russia, who had come to America at 19, a garment worker who embarrassed his son by speaking mangled English and shuffling when he walked (a sign of a spinal cord disease that Nuland abruptly recognized one evening while reading his physiology text at Yale). Nuland's father and adored mother had lost their first-born son before Sherwin, or "Shep," was born. And then Nuland's mother died, too, of rectal cancer, when he was 11.

Nuland was drawn to medicine both by his need to vanquish the disgust he felt about disease and because he revered doctors. "To me, as a child of 8, 9, 10, there was a nobility in a physician." In his chaotic world, physicians "had about them an equanimity that I genuinely admired, that was based on the reality that they really could do things, really could lift people up from the depths of despair and give them hope."

Indeed, a young physician effectively saved Nuland's life during his midlife depression. Nuland narrowly escaped a lobotomy because resident Vittorio Ferrero, M.D., protested the orders of his superiors at The Institute of Living in Hartford,

Conn. Nuland recovered after a string of electroshock treatments.

These days Nuland devotes all his time to writing and speaking. He's planning a trip to Shanghai this summer for the wedding of his son from his first marriage, and he has two young grandchildren by his older daughter, a NATO diplomat in Brussels. His two younger children, with actress and director Sarah Peterson, are of college age.

Nuland says his books have allowed him to become a kind of family physician in print. In that sense, he calls *Lost in America* "my ultimate book." "This is a kind of therapy for everybody who reads the book, to recognize that it's OK to be complex and confused. ... Because essentially what I'm saying is 'Look, look where I was, and look how I gradually came out of that to have made such a rewarding life.'"

—Cathy Shufro

A dinner guest inspires a mission to help former slaves

The night her husband brought a Sudanese guest home for dinner, **Cynthia Hymes Bell**, M.P.H. '84, heard a story that inspired her to risk her life. The visitor that night in October 1999 was Francis Bok, a 19-year-old who told of being abducted during a militia raid on a Sudanese village marketplace when he was 7 and spending the rest of his childhood as a slave.

Bell's husband, the Rev. Gerald E. Bell, had met Bok through his work as senior pastor at the Southern Baptist Church in Roxbury, Mass. "He was determined for me to hear Francis' story," recalls Bell. When Bok told of being captured, the Bells' 6-year-old son, Noah, began to cry. "That's not right," he said. "How can people take people?"

People do take people in Sudan: 10,000 to 17,000 people are currently enslaved there, according to estimates by UNICEF UK, most of them caught in the animist south and taken to the Muslim north.

Because he survived a decade of captivity (as an abused farmhand) and eventually escaped, Bok might even be counted as fortunate in the Sudanese context. Civil war lasting nearly 20 years has killed two million people and displaced twice that number in the nation of 37 million that lies south of Egypt.

The story that so upset Bell's son had a profound resonance for Bell as an African-American whose ancestors were themselves enslaved. Her sense of connection led her to join a trip to Sudan co-sponsored by the Zurich-based human rights group Christian Solidarity International, and My Sister's Keeper, a faith-based initiative based in Boston. In July 2002, Bell reports that she witnessed the "redemption" of about 1,200 people. For \$33 per person, the group bought back slaves from Arab northerners who make their living as "retrievers."

Bell's task was to talk to the tribal chiefs to find out what would happen to returnees without homes. "Many of them had no place to go. Their villages have been bombed, husbands have been killed, their children are missing. Where is home?" Some of the people may have lost their homes in raids by militias protecting Sudan's oil industry. Those militias have burned villages and killed and enslaved residents to clear the area along the pipeline into southern Sudan that brings in oil worth more than \$1 million daily. Complicating the situation is that southern rebels are fighting the junta in power.

Bell was relieved to hear that the chiefs would accept the strangers into their communities. She then interviewed the women to help them develop ideas for supporting themselves. They asked for a gasoline-powered grinding mill for grain.

A few weeks before her arrival, the spot where Bell camped had been bombed, and she lay stark

awake in her tent for three nights. "I questioned whether I would see my family again. ... Prayer kept me from totally freaking out." She believed she was in God's hands.

Bell and three other Boston-area women who have visited Sudan are researching prices for a grinding mill and consulting with contacts in Sudan about the safest place to locate it. "We're building relationships so we can go in and help, beyond the slavery issue," says Bell. Bell and the others in Boston, members of "My Sister's Keeper," speak about Sudan at churches and receive donations there. The next step, says Bell, is to use her public health training to develop a plan to respond to the threat and the effects of HIV.

—Cathy Shufro

Ten lines a day, for 78 years

Albert Doty Spicer, M.D. '37, D.M.D., was 13 when he wrote the first entry in his diary—and every day since, for 78 years, he's written 10 lines a day that record changes in 20th-century life. Spicer's diary served as the basis for a recently published history of his hometown of Westerly, R.I., that describes the mundane and the memorable, from playing mumble-the-peg to dancing in the streets on V-J Day in 1945.

Momentous Events in Westerly, Rhode Island includes historic photographs of the seaside town and Spicer's recollections: he watched the total eclipse of the sun—and saw a German dirigible on the same day—in 1925, the year he began writing. (He's never missed a day since, though he had to dictate his entries a few times following two strokes.) In 1927, when he was 15, he saw the *Spirit of Saint Louis* circle over Providence, R.I., and then glimpsed pilot Charles Lindbergh drive by in an open car. Spicer describes the hurricane of 1938, which washed away a swath of the resort towns of Weekapaug, Misquamicut and Watch Hill.

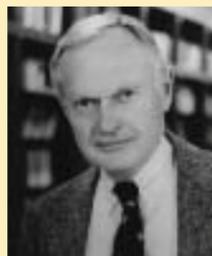
"Where there had been hundreds of houses, the beach was wiped clean. ..." Spicer also recalls after-school escapades, including *skijoring*, in which a trotting horse pulled people on skis behind it. Spicer writes about the night the Westerly Fire Station burned down in 1927. He describes his mother's cumbersome bathing costume, including stockings and shoes worn while swimming. When two-piece bathing suits first appeared in the 1930s, he recalls seeing a man on the beach "reading" an upside-down newspaper.

Although Spicer planned to study dentistry from the outset, he attended medical school because his father advised that a foundation in medicine would help him. An internship at Pawtucket Memorial Hospital allows Spicer to boast, "I'm the only dentist who's delivered 60 babies." After earning his dental degree at Harvard, Spicer set up an office in the town where his father and grandfather had served as dentists before him. His son, Albert D. Spicer Jr., was in his final year of dental school when he was killed in a car accident in 1965. Spicer's daughter, Judith Spicer Knutson, helped assemble the book.

Spicer said the biggest change he saw during his career was the evolution from corrective to preventive dental care. He experimented with using music as an alternative to anesthesia. Spicer said the technique worked for most patients but never caught on. Anesthesia with a needle seems simpler and quicker to most dentists, he says.

Spicer lives by the Atlantic on Weekapaug Point in Westerly. He gave up skiing six years ago, at age 85, and has sold his sailboat, but he and his wife, Marion, welcome invitations to crew. Spicer has simple advice about what we should all be doing for our teeth: "Hang onto them!"

—Cathy Shufro



Sherwin Nuland



Cynthia Bell



Albert Spicer

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 yymm@yale.edu or write to Faces, Yale Medicine, P.O. Box 7612, New Haven, CT 06519-0612.



Carl Andrews



Martin Robson



Frederick Sherman



Audrey Weiner



Robert Higgins

1940s

Carl E. Andrews, M.D. '44, retired and living in Port St. Lucie, Fla., is now a "gentleman farmer" with 103 orange and grapefruit trees. He handles the farm completely by himself, including the cultivation, pruning and picking in early spring. After harvesting his crop, he travels through the neighborhood on his bicycle distributing bags of complimentary fruit. Andrews' residence is in a neighborhood built around a small airstrip. The development was designed for individuals who own small planes, and each backyard has an aircraft taxi road leading to the airstrip. Although robust for his years, Andrews gave up his plane and license several years ago because of his age.

1970s

Martin C. Robson, M.D., HS '73, professor emeritus of surgery at the University of South Florida in Tampa, was awarded an honorary fellowship in the Royal College of Surgeons of England in July 2002. Robson, one of three recipients and the only honoree from outside the United Kingdom, was on the faculty at Yale until August 1974. Previous awards include an honorary fellowship in the Royal Australasian College of Surgeons, the Lifetime Scientific Achievement Award of the Wound Healing Society and the Distinguished Service Award from the American Burn Association.

Frederick S. Sherman, M.D. '75, professor of pediatrics and obstetrics and gynecology at the University of Pittsburgh School of Medicine and the director of Perinatal Cardiology at Magee-

Womens Hospital, a department that he founded in 1988, writes to say: "Like many I was exasperated by inefficiencies in academic medicine and communication issues between medical staff and administration. So ... I went to business school and I am happy to report I received my M.B.A. from the Katz Graduate School of Business at Pitt in December 2002." His department is devoted to diagnosing and managing cardiac problems in fetuses, newborns and pregnant women.

Audrey S. Weiner, D.S.W., M.P.H. '75, was appointed president and CEO of The Jewish Home & Hospital LifeCare System in November. Her responsibilities include leading the System's three campuses, in Manhattan, the Bronx and Westchester, N.Y. She also assumes supervision of the Lester Eisner Jr. Center for Geriatric Education, the Kathy and Alan C. Greenberg Center on Ethics in Geriatrics and Long-Term Care and the Center on Pharmacology/Pharmacy for the Elderly.

1980s

Robert S.D. Higgins, M.D. '85, former chair of cardiothoracic surgery and professor of surgery at the Medical College of Virginia, Virginia Commonwealth University, in Richmond, was appointed chair of the department of cardiovascular-thoracic surgery at Rush-Presbyterian-St. Luke's Medical Center in Chicago in January. His focus at Rush will be to enhance and advance the care of patients with diseases of the heart and lungs.

The Ohio Rural Developmental and Behavioral Clinic Initiative, directed by **Ronald L. Lindsay, M.D.**, HS '86, received the 2003 Ambulatory Pediatric Association Health Care Delivery Award in May. The award recognizes innovative and effective programs that provide health care in a teaching setting, and outstanding programs or systems of health care. The program provides referrals, training in the health professions and coordination of care by public health nurses in conjunction with local pediatricians.

Antoinette L. Lloyd, M.D. '86, is a family physician and director of Healthy Jacksonville, part of the national Healthy People 2010 preventive medicine project for Jacksonville, Fla. She has been married for 18 years to **John M. Montgomery, M.D.**, M.P.H. '84. Montgomery is director of health services and chief medical epidemiologist for Jacksonville, and a program director and assistant professor of community health and family medicine at the University of Florida.

2000s

Joanna B. Sheinfeld, M.D. '00, a resident in internal medicine at Mount Sinai Hospital in New York City, was married on February 16 to Mark D. Paltrowitz, a director of portfolio analysis with BlackRock Inc., an asset management company in New York.

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Franklin C. Behrle, M.D. '46, of Grantham, N.H., died October 6 of renal failure due to diabetes. He was 80. Behrle, professor emeritus and chair of pediatrics at the University of Medicine and Dentistry of New Jersey, was co-founder and executive chair of the Statewide Perinatal Services and Research Center.

Ronald C. Brown, M.D. '74, of South Orange, N.J., died August 14. Brown, whose practice was in internal medicine, was a former vice president of medical affairs at Oxford Health Plans in Edison, N.J.

Joseph Budnitz, M.D. '34, former chief of cardiology at the Berkshire Medical Center in Pittsfield, Mass., died on October 7 of cardiac arrest at the age of 93. In 1941, he was among the first physicians certified by the newly formed American Board of Cardiovascular Disease.

Harrison Dunn, M.D., HS '63, of Visalia, Calif., died on October 15 in Pixley, Calif., at the age of 73. For most of his career Dunn was an emergency room physician at the Veterans Memorial Medical Center in Meriden, Conn. He retired in 1993 and moved to California, where he was employed by the state as a physician at the Corcoran Prison.

Stephen Fleck, M.D., professor emeritus of psychiatry and public health at Yale, died on December 19 at the age of 90. Fleck served as psychiatrist-in-chief of both the Yale Psychiatric Institute and the Connecticut Mental Health Center and was known for his influential research work on schizophrenia and the family.

During World War II he helped to evacuate and treat concentration camp prisoners and to interrogate German prisoners.

William W. Glenn, M.D., former chief of cardiothoracic surgery at the medical school, died on March 10 at Monadnock Community Hospital in Peterborough, N.H. He was 88.

In 1950, using a pump made from parts of a child's Erector set, Glenn and colleague William H. Sewell, M.D., created a mechanical heart pump, the forerunner of heart-lung bypass machines. Four years later Glenn became the first to use a vena cava-pulmonary artery shunt to bypass malformed hearts in the treatment of blue babies. And in 1959, Glenn and colleagues introduced the concept of electrical stimulation by radio frequency induction into medical practice, first used to pace the heart and later the diaphragm. Glenn's textbook, *Glenn's Thoracic and Cardiovascular Surgery*, now in its sixth edition, has become the international standard text for vascular surgeons.

Elizabeth R. Harrison, M.D. '26, one of the first women to graduate from the School of Medicine and pediatrician to three generations of New Haven children, died in her sleep on January 5 at the age of 103.

Charles A. Janeway Jr., M.D., professor of immunobiology at the School of Medicine and a Howard Hughes Medical Institute investigator, died on April 12 at age 60 in New Haven after a long illness. One of the leading immunologists of his generation, he developed many of the concepts that are

the basis of immunology today. He is renowned for his recent work on innate immunity, the body's first line of defense against infection.

Janeway predicted in 1989 that pattern recognition receptors would mediate the body's ability to recognize invasion by microorganisms. This prediction was made first on theoretical grounds, and subsequent experimental work established the underlying mechanisms.

Janeway published more than 300 scientific papers and was the principal author of the acclaimed textbook *Immunobiology: The Immune System in Health and Disease*, now in its fifth edition.

Ernest R. Kimball, M.D. '36, of Jacksonville, Fla., died December 27 at the age of 93. A pediatrician dedicated to the benefits of breastfeeding, Kimball helped found the Evanston (Ill.) Hospital Breast Milk Bank. Kimball and his wife, Alicia, co-founded a not-for-profit ranch in Zion, Ariz., providing physical and recreational therapy for children with mental and physical disabilities.

Samuel Reback, M.D. '25, a retired neurologist and psychiatrist, died November 22 in New Smyrna Beach, Fla., He was 101. Reback, a former resident of Staten Island, N.Y., was an expert in mental illness and neurological disorders and testified at trials. He wrote many papers on neuropsychiatry and was the first to describe the disorder known as Familial Paroxysmal Choreoathetosis.

Priscilla Taft, M.D. '44, of Lenox, Mass., died November 23 at the age of 85. Taft was a pathologist

at Massachusetts General Hospital. She graduated from Radcliffe College but was turned down for admission by the Harvard Medical School because they would not accept women. While at Yale she contracted tuberculosis, an occupational hazard for medical students, and met her husband, Edgar B. Taft, M.D. '42, while both were in treatment.

Arnold D. Welch, Ph.D., M.D., former chair of pharmacology at Yale, died at home in San Diego on October 11 at the age of 94. Welch also served as department chair at Western Reserve University and was president of the Squibb Institute for Medical Research. At age 75, Welch joined the National Cancer Institute to coordinate the National Cooperative Drug Discovery Groups and served as acting deputy director of the division of cancer treatment.

C. Bruce Wenger, M.D. '70, Ph.D. '73, of Natick, Mass., died November 22 after a long illness. He was 60. A pharmacologist, Wenger had been a medical researcher for the Army, specializing in heat-related illnesses. He loved to sing and belonged to the Stambandet Swedish Singing Group and the Norumbega Harmony Singers. Wenger was a long-standing member of Gideons International, the oldest Christian business and professional men's association in the United States, and the Park Street Church Missions Committee.

SEND OBITUARY NOTICES TO
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to claire.bessinger@yale.edu



Rolling on outa here

When warm weather beckoned this spring, genetics graduate student Matthew Weed joined fellow students studying outdoors for the first time in his six years at the School of Medicine. Weed, who is blind, used new wireless technology for his Macintosh laptop to listen to articles being read aloud and to check his e-mail—all in the semibucolic setting of the Harkness Courtyard.

Weed is close to completing the dissertation on science and public policy that was just taking shape when he was profiled by *Yale Medicine* three years ago ["Bringing Science Into Focus," Summer 2000]. He is studying "what society decides to do about controversial research: how to regulate it, how to assimilate it." Part of his analysis compares how policy-makers in the United States and the United Kingdom regulate scientific research in areas such as stem cells and cloning. "Different countries come to different policy-making decisions. Why? I'm interested in the decisions themselves and what the mechanisms and who the contributors were."

Weed could have studied this topic in a political science department, but he says he would have missed an important element: "exposure to how scientists think about science and how physicians think about medicine." He said researchers are very reluctant to confront the fact that the practical uses of their discoveries may frighten or repel society. Scientists fear that if potential problems are made salient, they'll lose their freedom, says Weed.

But facing these issues is not optional, Weed argues. "No single government can stop knowledge from being created." The challenge is "how to assimilate knowledge even if we're uncomfortable with it."

Weed hopes to find a job in Washington with a large corporation or a government policy-making agency. He is considering strategies for how to incorporate medical support for his diabetes into his daily life once he leaves the university, where volunteer students monitor Weed's glucose levels and inject insulin twice daily. When he's away from his laptop, Weed still goes inline skating (with a friend to guide him), and he plans this summer to try water skiing for the first time.

—Cathy Shufro



WINTER 1968

"Alumni and particularly former house staff will be pleased to learn that the stipends for interns and residents at Yale-New Haven Hospital were increased January 1, 1968, and there will be a further increase effective July 1. The January change raised interns from \$4,000 to \$5,000 per year; new stipends for residents range from \$5,500 to \$8,000 per year.

"For the 1968-1969 house staff year beginning in July, interns will receive \$6,000; assistant residents, first year—\$6,600, second year—\$7,200, third year—\$7,800; fourth year residents, \$8,400; and chief residents, \$9,100.

"The cost of a medical education, however, continues to rise along with the general inflationary spiral. The present \$1,900 annual tuition at the Yale School of Medicine will increase to \$2,150 as of September, 1968. This is equal to the tuition now charged at many other private medical schools and, incidentally, is less than the 1968 tuition at some schools. The total cost for attendance for four academic years at a privately supported medical school is estimated to be at least \$16,000."



SPRING 1991

"Both adults and children can now be treated at Yale for vascular tumors of the skin, thanks to the new pulsed dye laser acquired by the School of Medicine and Yale-New Haven Hospital.

"This laser—the only one of its kind in the region—treats port-wine stains as well as other blood vessel tumors and broken blood vessels. Port-wine stains, like the purplish-red birthmark on the forehead of Soviet President Mikhail S. Gorbachev, occur in three out of every 1,000 newborns. ...

"The laser unit, about the size of a small washing machine, uses fiber-optic cable to conduct the laser energy. Patients require no anesthesia for the treatment, which feels like the snap of an elastic band. In most cases, vascular tumors can be permanently removed, although several treatments may be required."

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