Yale Medicine

autumn 2005

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The unseen wounds of war

ON THE COVER

A Marine rests during operations in Parwana, Iraq, in August. The Marines were seeking insurgents in the western Iraqi town just days after a roadside bomb killed 14 of their comrades.

BACKGROUND

Soldiers guard the scene of an attack on an armored personnel carrier, still blazing in the distance, in West Baghdad in April.

AP/Wide World Photos

On the Web yalemedicine.yale.edu

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

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Letter from Kathmandu

In January 2004 Johnnie Yates, M.D. '95, took a job as a physician in an international clinic in Kathmandu, where a typical day provided insights into medicine in Nepal. *By Johnnie Yates, M.D.* '95

The unseen wounds of war

As long as humans have waged war, the horrors of the battlefield have caused psychological damage. As troops return from Iraq, therapists, psychiatrists and veterans of previous wars are helping them return to civilian life. By Cathy Shufro

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Working in a Yale laboratory in the 1940s, Dorothy Horstmann solved a puzzle that would lead to the first polio vaccine. *By David M. Oshinsky, PH.D.*

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Since he arrived at Yale in 2004, Dean Robert Alpern has led faculty to a new vision of the medical school, with a focus on clinical expansion and the application of great science. *By Michael Fitzsousa*

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Article ignored ethical aspects of stem cell research

I was disappointed with the Chronicle piece by Marc Wortman ["For Stem Cell Researcher, Connecticut's Initiative Offers a New Avenue for Progress," Summer 2005] that involved an interview with Diane Krause, M.D., PH.D., and focused on her support for human embryonic stem cell research.

The superficial approach of the article minimized the ethical controversies of human embryonic stem cell research and offered readers an unbalanced and misleading feelgood article.

Lacking was acknowledgement that, with the technology currently available, human embryonic stem cell research involves the destruction of human embryos. As a former human embryo myself writing to another former human embryo (yourself), it should not need to be stated that human beings come from human embryos, but advocates of human embryonic stem cell research seem unwilling to acknowledge this basic biological fact. I was particularly chilled by Dr. Krause's statement that she wants "the freedom to use embryonic stem cells as a tool." I think the piece should have noted that there exist some serious and complicated moral and ethical concerns in this type of research even if Dr. Krause is seemingly not troubled by them.

If anything, Dr. Krause's own work with adult stem cells suggests that we have much to gain from that line of research, which does not have the same moral and ethical difficulties as research with human embryonic stem cells. The article failed to mention that to date thousands of living patients have been helped with adult stem cell technology. This includes patients with spinal cord injuries, genetic and metabolic disorders, impaired heart function and so on. It did not mention that no one has yet been helped in any way by embryonic stem cells.

I would like to have seen a better analysis of these grave and pressing issues in your magazine. I hope Yale Medicine will take on this controversial topic in a more comprehensive manner with a future feature article. Robert Kaladish, M.D. Amherst, N.H.

Article on schistosomiasis was inspiring

I want to congratulate Kohar Jones for her impressive and beautiful article ["The Silent Scourge of Development," Summer 2005], and you, for publishing it. Especially in this period when greed and deception are often so dominant, to see something like that article is particularly inspiring and a reminder that there are wonderful people in this world, young as well as old. Please pass my comments on to her. She deserves any recognition she gets. John Strauss, м.D.

Professor emeritus of psychiatry New Haven

Ibn Sina's roots

I enjoy reading the articles in Yale Medicine very much and I think the magazine offers an excellent selection of topics.

Just as a quick note, in the mustard gas article ["From the Field of Battle, an Early Strike at Cancer," Summer 2005], you refer to Ibn Sina, the 10thcentury physician and scholar. He was actually Persian, not Arab. The reason he wrote in Arabic was that the official language for science in Iran was Arabic after the Arabs conquered the Persian Empire.

Thanks again for the excellent ideas and articles!

Setareh Vistamehr, M.D. Instructor, Department of Ophthalmology and Visual Science New Haven

As Dr. Vistamehr notes, Ibn Sina, known as Avicenna in Europe, was not an Arab. Because he was born in what is now Uzbekistan and died in what is now Iran, his roots are a subject of debate. For more on Avicenna, see "From the Middle East, in the Middle Ages," p. 16, in this issue. —Eds.

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Nostalgia of another kind

In 1980, years after the last troops returned home from Vietnam, the military and medical establishments put a name on the psychiatric sequelae that have afflicted soldiers for as long as there has been war—post-traumatic stress disorder (PTSD). Documented since the time of Homer and variously known as nostalgia, combat fatigue and shell shock, it is marked by anxiety, flashbacks, irritability and withdrawal from society, among other symptoms. In our cover story we examine PTSD and its implications for troops coming home from Iraq. To find out what has been learned about PTSD and how the experience of Vietnam veterans is helping today's troops, writer Cathy Shufro spoke with Vietnam and Iraq veterans as well as psychiatrists and social workers at Yale and the VA Connecticut Healthcare System in West Haven.

We also look back half a century to the days when parents kept children away from public pools and beaches in the summertime. Polio was a dread disease, but scientists were getting closer to discerning how it acted and how to prevent it. Among those scientists was the late Dorothy M. Horstmann, M.D., FW '43, a member of the Yale Poliomyelitis Study Unit, who made a key discovery about polio antibodies that paved the way for development of vaccines. We asked David M. Oshinsky, PH.D., a historian at the University of Texas at Austin, and author of *Polio, An American Story*, to profile the first woman to become a professor of medicine at Yale.

Finally, in this issue we profile Robert J. Alpern, M.D., who took over as dean almost a year and a half ago. As *Yale Medicine*'s editor, Michael Fitzsousa, reports, Alpern has spent the time assembling his management team, getting to know the medical school and launching a strategic plan to move the school forward.

John Curtis Managing Editor john.curtis@yale.edu

SECOND OPINION BY SIDNEY HARRIS



"... AND IF YOUR SYMPTOMS DISAPPEAR WITHIN THREE DAYS, I'LL GET A LARGE GRANT."

A mouse offers a new way to test vaccines

By implanting a human immune system into mice, scientists plan to study vaccines.

The laboratory mouse-resilient, easy to breed and ideally suited to the genetic manipulations that form the basis of much of modern biomedical researchhas been invaluable to immunologists such as Richard A. Flavell, PH.D., chair and Sterling Professor of Immunobiology. But there are limits to the usefulness of this most versatile of research animals in immunology, because the mouse immune system has been tailored over evolutionary time to deal with pathogens different from those that infect humans. To compensate, scientists like Flavell supplement their work in mice with studies of human immune cells in culture, but here, too, there are inherent compromises. The immune system, a multifaceted mechanism distributed throughout the body, is difficult to emulate in a petri dish, and the behavior of cells in culture can be a poor predictor of how a drug will work in the living human body.

Since ethical considerations prohibit testing drugs in humans before they've been proven safe and effective, these intrinsic limitations of the tools available to immunologists mean that bringing vaccines and other cures from the laboratory to the clinic often requires a leap across an unavoidable knowledge gap.

"You don't really want to be studying mouse cells; you want to study human cells, and ultimately you study humans in clinical trials," said Flavell, who is also a Howard Hughes Medical Institute investigator. "There are enormous difficulties making sure that what you do in clinical trials is safe and isn't going to adversely affect the patient."

But a remarkable advance in a Swiss laboratory may provide a longsought bridge between the bench and the bedside for immunologists. In 2004, Markus G. Manz, M.D., and



colleagues at the Institute for Research in Biomedicine created a rudimentary human immune system in mice by injecting human umbilical-cord blood containing stem cells and other progenitor cells into a mutant strain of mice that lack immune systems.

Manz's paper appeared just as the Grand Challenges in Global Health initiative was accepting final proposals for grants. The initiative, funded by the Bill & Melinda Gates Foundation, the Canadian Institutes of Health Research and the Wellcome Trust, and administered by the Gates Foundation, planned to distribute more than \$436 million to support innovative research on diseases that afflict the world's poorest people. Flavell proposed that his team join forces with Manz and with Tarrytown, N.Y.based biotech company Regeneron Pharmaceuticals to perfect a mouse model of human immunity for testing vaccines. In late June, Flavell learned that the initiative would award \$17 million to the project.

"It's akin to a 'Manhattan Project,' to make this work like a true human immune system, so you could really do experimentation that is predictive of the human response," Flavell said.

A mouse model of human immunity, for example, would allow scientists to test a vaccine for HIV, which has heretofore been impossible because mice are normally not susceptible to the virus. But Flavell said that the technique will have any number of applications. "This system, once it's up and running, could be used to study all kinds of things," he said.

Elizabeth E. Eynon, PH.D., a research scientist in Flavell's lab, said that the model could make clinical trials much more efficient. "The FDA will require people to do just as many Phase I and Phase II trials as they do now," she said, "but the likelihood of failure at those stages would be reduced if we can show safety and efficacy beforehand."

—Peter Farley

Marna Borgstrom named to lead Yale-New Haven Hospital and Health System

Since she joined Yale-New Haven Hospital (YNHH) as a junior administrator in 1979, Marna P. Borgstrom, M.P.H. '79, has become a vice president, the chief operating officer and, as of October 1, the CEO and president of the hospital and the Yale New Haven Health System (YNHHS). She succeeds Joseph A. Zaccagnino, M.P.H. '70, who retired on September 30 after a 35-year career at the hospital.

During more than a quarter-century at the hospital she has watched it grow into the 944-bed flagship of a health system that stretches along Long Island Sound from Rye, N.Y., to Westerly, R.I. It is the hub of a New Haven health care delivery network that includes a children's hospital, a psychiatric hospital, two independent ambulatory surgical centers, a large radiology practice and the Shoreline Medical Center in Guilford.

Working with Zaccagnino, Borgstrom oversaw the hospital's \$850 million budget and served as the primary liaison to the School of Medicine. She led the planning and construction of the children's hospital, and headed up a patient safety program that trained 40 senior managers under General Electric's process-improvement initiative known as Six Sigma. As the secondin-command at the hospital for more than a decade, Borgstrom helped develop YNHHS, an affiliation of several dozen organizations including умнн and two other large hospitals, in Bridgeport and Greenwich, that encompasses their networks of physician practices, surgical centers, diagnostic facilities, rehabilitation centers, pharmacies and visiting nurses.

"We want to be the provider of choice—locally, of course, but also regionally and nationally," she said. The hospital's regional and national distinction, which Borgstrom intends to build on, reflects joint investments in unique clinical programs with the School of Medicine. She is looking forward to the construction of a \$440 million clinical cancer center, cur-rently awaiting approval from New Haven zoning officials, that will provide needed capacity for current and emerging clinical initiatives.

Other recent achievements of YNHHS include the creation of an emergency angioplasty program at Greenwich Hospital in collaboration with YNHH and physicians at the School of Medicine. Previously, emergency patients in Greenwich had to be transported out of town for the procedure. Now they can be treated locally, and elective angioplasty cases and cardiac surgeries will be referred from Greenwich to New Haven.

A revamped liver transplantation program that began operations in July has the potential to draw pediatric patients from the region and beyond, and many joint programs—in epilepsy, endocrine surgery and maternal-fetal medicine, to name several—already bring patients to New Haven from across the country. Borgstrom would like to see the list grow, so that more out-of-state patients come to the city for care.

Her appointment came a little more than a year after the arrival of medical school Dean Robert J. Alpern, M.D., in



June 2004. Based on her work with Alpern during his first year here, Borgstrom sees "unprecedented opportunities" ahead for the hospital and medical school. Alpern called Borgstrom "an excellent choice for the job of CEO."

Borgstrom earned her public health degree in hospital administration at Yale in 1979. She said the program gave her a footing in how to analyze and solve problems at a large health care organization, and also an appreciation for the public health challenges facing health care executives.

—Michael Fitzsousa



Artist Laura Ferguson uses medical images in her Visible Skeleton Series, which was displayed at the National Museum of Health and Medicine in Washington in the spring of 2005. This work from the series incorporates oils, bronze powder, charcoal, colored pencil, pastel and oil crayon on paper.

Portraits in light artists blend medical imagery into their work

In the 1990s, when Bettyann H. Kevles, M.A., asked listeners of the National Public Radio program *Science Friday* to imagine their bodies intertwined with medical technology, she received seven responses, all from artists. All seven had experienced imaging techniques such as X-rays, magnetic resonance imaging, computed tomography (CT) scans and other routine procedures. One described them as "portraits in light."

A lecturer in Yale's Program in the History of Medicine and Science, Kevles studies how new technologies become a part of everyday life. But having grown up in a family of painters and having studied painting herself, Kevles has a long-standing interest in art. Over the years, she has built up a library of work by visual artists who explore their medical conditions in their paintings. She explored this theme, in part, in her 1997 book, Naked to the Bone: Medical Imaging in the 20th Century, and in Picturing DNA, written with Marilyn Nissenson and published online in 2000.

At a symposium on brain imaging at the annual meeting of the American Association for the Advancement of Science in Washington in February, Kevles presented the work of visual artists who had used medical imaging to create self-portraits. The survey reached back to the early 20th century and the work of Mexican painter Frida Kahlo, whose spine was severely injured in an accident when she was an 18-yearold student, and whose self-portraits show her body and spine from the inside in a manner reminiscent of Xrays. Many contemporary artists have incorporated more modern techniques. New York artist Laura Ferguson, who suffers from scoliosis, studied anatomy, consulted with orthopaedic surgeons and radiologists and imaged her body with a 3D spiral CT scan, which allowed her to visually manipulate her skeleton to observe it from different angles and in different postures. Her Visible Skeleton Series, a visual autobiography created by blending many layers of colors on paper, was on display at the National Museum of Health and Medicine in Washington this spring.

Since writing her 1997 book, Kevles has continued her study of artists such as Jennifer Hall of Boston, who has temporal lobe epilepsy and used an electroencephalogram to capture her brain waves during a seizure. She then used a computer program to transform the erratic spikes into a three-dimensional image and cast it in silver in the shape of a tiara.

In her more recent work, Kevles has explored the idea that turning medical imaging techniques into tools of self-exploration allows artists to work through their illness so they can get past seeing themselves as victims of it. "Having seen whatever it is plaques in their brain, or an EEG of a crazy electrical storm—they no longer think of themselves as epileptics, for example. They're people with particular parts of their bodies that don't work," Kevles said. "Many artists feel that their art, in this way, gives them power over their conditions."

—Alla Katsnelson



GREY NAMED DEAN OF NURSING

Margaret Grey, R.N., DR.P.H., was named dean of the School of Nursing in July. Grey, previously associate dean for scholarly affairs, joined the faculty in 1993. She succeeds Catherine L. Gilliss, D.N.SC., who served as dean from 1998 until last year. Grey, an internationally known researcher in the natural history of adaptation to chronic illness in childhood, is the author of more than 160 publications.

Yale endowment earns 22 percent, as investment steward earns plaudits

News of outstanding returns on Yale's endowment came as the university's chief investment officer was already riding a wave of favorable publicity. David F. Swensen, PH.D. '80, had recently published his book Unconventional Success: A Fundamental Approach to Personal Investment (Free Press), and finance journalists were calling him the best money manager in academia. They pointed to Swensen's track record as manager of Yale's endowment over the past 20 years, which has seen average returns of 16 percent. For the 2004 fiscal year, the endowment earned returns of 22.3 percent, bringing total assets to \$15.6 billion. And under Swensen's leadership, the Yale endowment routinely outperforms Standard & Poor's 500. He credits his success to a nontraditional asset allocation with an emphasis on equity investments.

In numerous interviews with the press, however, Swensen cautioned that

individual investors are unlikely to reap his returns, even if they read his book. Those who spend a few hours a week on their portfolios simply can't compete with institutions such as Yale that have a team of full-time professionals actively managing the endowment.

"The outstanding performance by the investments office in the past year has matched a record of achievement over time that has earned David Swensen and his colleagues the highest possible praise and admiration from their peers," President Richard C. Levin said in a press release. "Yale's capacity to fulfill its ambitious mission has been greatly enhanced by their superb stewardship of the endowment."

Because of Swensen's efforts, the endowment's share of the university's operating budget has more than doubled over the past decade. The endowment now contributes almost a third of the university's revenues—\$610 million this fiscal year—the largest single source of support.

—John Curtis

et cetera ...

GOLDMAN-RAKIC FELLOW NAMED

Susheel Vijayraghavan, a graduate student in neurobiology at the School of Medicine, has been selected as the recipient of the 2005 Patricia S. Goldman-Rakic Fellowship. This fellowship, established by Yale and the pharmaceutical maker Pfizer in 2003, honors the memory of the late Yale professor Patricia Goldman-Rakic, PH.D., and highlights excellence in neuroscience research at the medical school. According to Lynn Cooley, PH.D., director of the Combined Program in the Biological and Biomedical Sciences, Vijayraghavan's selection is a "tribute to Dr. Goldman-Rakic's distinguished career and to Susheel's developing career."

Vijayraghavan studies the effects of dopamine on working memory in primates and was Goldman-Rakic's final graduate student before her death in 2003. As the fellowship recipient, he will receive tuition, a stipend and health care coverage, as well as additional funds for travel to scientific meetings. —J.C.

YALE WEBSITE DESIGNERS HONORED

Patrick J. Lynch, M.S., director of the Med-Media Group of Yale's Information Technology Services, and C. Carl Jaffe, M.D., professor of medicine (cardiology), received the 2005 Pirelli Prize for Multimedia Education and the Top Pirelli Prize for 2005 for the educational website "Introduction to Cardiothoracic Imaging." The prizes, which they received in Rome in June, honor technical innovations and contributions to science education through the outstanding communication of science and technology.

The Pirelli S.p.A. Group, one of Europe's major telecommunications and manufacturing firms, has underwritten the awards since their inception in 1996. The Pirelli jury cited the extraordinary depth and breadth of the cardiothoracic imaging site (http://info. med.yale.edu/intmed/cardio/imaging).

"At no time in history does the intersection of media and science education matter more," said Jaffe, who retired in July after 35 years on the faculty of the School of Medicine. "Ignorance of or, more importantly, denial of the truths of science obscures recognition of our common humanity."

[—]J.C.



Biomarkers warn of a "silent killer"

High or low levels of certain proteins can signal the likelihood of ovarian cancer.

Epithelial ovarian cancer ranks as the most lethal of gynecological malignancies. It is only 10 percent as common as breast cancer, but its mortality rate is three times as high. The reason is simple: routine mammography and breast examinations can catch breast cancer early, but no such screening exists for ovarian cancer in its early stages. With few early symptoms, the disease passes under the medical radar until it has reached later stages of malignancy, and therapeutic options are often limited.

Now a group headed by Gil Mor, M.D., PH.D., associate professor of obstetrics, gynecology and reproductive sciences, has found a way to detect the "silent killer" in its earliest stages, according to a report in May in the Proceedings of the National Academy of Sciences. The researchers at Yale, George Washington University and the Nevada Cancer Institute devised a still-unapproved screening test that measures levels of four cancer-related proteins-leptin, prolactin, osteopontin and insulin-like growth factor II (IGF-II)-in blood samples. These biomarkers are proteins that change in response to several different forms of cancer, perhaps as part of the immune response. "Our strategy is unique in that we are using a combination of proteins representative of how the total system reacts to cancer, rather than focusing on one protein," said Mor.

Previous studies had identified each of the four proteins as possible biomarkers, but Mor's team found that individually none of the proteins served as a reliable indicator of cancer.

The researchers began with 169 proteins linked to epithelial ovarian cancer. They then narrowed the list to 35 proteins that were either far more or far less prevalent in women with advanced cancer than in healthy women. They further refined the biomarker pool to the four proteins, two of which are consistently overproduced (prolactin and osteopontin) and consistently underproduced (leptin and IGF-II) in women with cancer.

To put these findings to clinical use, women need only have blood drawn. Levels outside of the normal range of two or more of the biomarkers predict cancer. Follow-up analyses, such as ultrasound, can verify the diagnosis.

In a preliminary study of more than 200 women, the screen accurately detected ovarian cancer in 95 percent of cases. The specificity of the testthose correctly diagnosed as diseasefree—also stood at 95 percent, but Mor stressed that the test is not ready for screening the general population. "Because this disease is relatively rare, a specificity of 95 percent means that 5,000 out of every 100,000 women tested by this method would give a false-positive result. That's not acceptable," he said. To increase the screen's specificity to an acceptable 99.6 percent, Mor's team is looking at adding three more proteins to the biomarker pool.

—Kara Nyberg

8

With the Canary Database, animals become sentinels for environmental hazards

Before the effects of mercury poisoning showed up in the children of Minamata, Japan, in the 1950s, cats were getting sick with a neurological ailment dubbed "dancing cat disease." In Africa, human outbreaks of the lethal Ebola virus follow the dying off of animals including apes and deer. And epidemiologists are keeping a watchful eye on avian flu, which has jumped from chickens to humans in Asia and Europe.

Since 2002 an interdisciplinary group of researchers at Yale has been creating a database that makes the connections between diseases in animals and diseases in humans. With funding from the National Library of Medicine, the Canary Database hopes to harness this information so that animals can serve as sentinels of impending human disease.

"If you have an animal that is sick from an environmental hazard, should human health professionals be concerned?" asked Peter M. Rabinowitz, M.D., M.P.H. '95, FW '98, associate professor of medicine and principal investigator of the database. The question is not hypothetical. It was a veterinarian at the Bronx Zoo who in 1999 reported the occurrence of dead crows to public health authorities, who did not initially recognize that the birds were signaling the emergence of West Nile virus in this hemisphere. "That is a good example," Rabinowitz said, "of the communication barrier and world-view barrier we are trying to bridge."

In order to overcome gaps between experts in animal health and those in

human health, the Canary Database makes animal sentinel studies from a variety of biomedical databases easily accessible. Researchers can search the database for a wide variety of environmental hazards, both toxic and infectious; learn how these hazards have been studied in animal populations; and discover whether there is evidence linking the animal disease event to human health risk.

The database takes its name from the proverbial canary used by coal miners to warn of the presence of carbon monoxide. A collaboration of the Yale Occupational and Environmental Medicine program, the Yale Center for Medical Informatics and the U.S. Geological Survey National Wildlife Health Center, the database culls from veterinary literature papers on animal disease that might have relevance to humans. Five curators, including veterinarians and physicians around the country, review and curate the papers, adding information about epidemiological methods and linkages to human health outcomes.

The information they collect could be used to help public health practitioners detect impending disease outbreaks or terror attacks involving chemical or biological weapons. "We want to be a continuing resource," Rabinowitz said.

-John Curtis



et cetera ...

ALCOHOL LOWERS CANCER RISK

The incidence of non-Hodgkin's lymphoma (NHL) is rising throughout the world—in industrialized nations it ranks as the sixth most common cancer among men and the eighth most common among women. Although studies have suggested that alcohol consumption may lower the risk of NHL, results have been inconsistent.

In July a team at the Department of Epidemiology and Public Health reported in the journal *Lancet Oncology* that alcohol consumption does indeed lower the risk of NHL. Unlike prior studies, this one pooled data from nine studies covering more than 15,000 people in the United States, the United Kingdom, Sweden and Italy. "This study with a large sample size allows us sufficient statistical power to analyze the data by type of alcohol consumed and disease subtype," said principal investigator Tongzhang Zheng, SC.D., professor of epidemiology.

Further studies are needed to explore the link between alcohol consumption and the lower risk of NHL. —J.C.

MUSIC AND SEDATIVES

For decades, doctors and nurses in the operating room have turned to music to soothe the nerves of anxious patients. Several studies have found that patients who listen to music are less anxious before surgery and need less anesthesia.

But Zeev N. Kain, M.D., HS '92, FW '93, professor of anesthesiology, pediatrics and child psychiatry, wondered whether music did more than simply drown out the racket in the operating room. With colleagues at Yale and the American University of Beirut in Lebanon, he designed a study in which patients who had received spinal anesthesia—but were awake—could control the dosage of a sedative. They listened through headphones to either music of their choice or white noise generated by a relaxation device. As reported in May in the journal Anesthesia and Analgesia, patients who listened to music used significantly less sedative.

"Doctors and patients should both note that music can be used to supplement sedation in the operating room," Kain said. —Peter Farley

A moth's gene helps discern gene functions

A piece of DNA from a moth could signal a major leap in the understanding of what specific genes do.

A new tool for genome research, developed in the Yale laboratory of Tian Xu, PH.D. '90, professor and vice chair of genetics, professor of molecular oncology and development and a Howard Hughes Medical Institute investigator, promises to greatly accelerate the work of assigning purpose to thousands of unexplored human genes.

The tool is a jumping gene, a small piece of DNA called a transposon that moves around the genome, usually settling in other genes and allowing scientists to suppress the activity of existing genes or insert new ones.

Transposons are active in many plant and insect genomes and have helped to make the fruit fly *Drosophila* the darling of geneticists, as these mobile DNA fragments were used to decipher the role of nearly every gene in that model organism. But for decades scientists could not find an equivalent transposon for mammals.

As reported in the August 12 issue of the journal *Cell*, Xu and his colleagues manipulated a transposon called *piggyBac*, found in the cabbage looper moth, so that it can be easily cut and pasted into the genomes of higher organisms, including mice and humans. "With this transposon, we now have the ability to systematically inactivate each and every gene in a model organism like the mouse," Xu said.

In mouse studies, scientists have traditionally used chemicals to modify genes, but this approach is painstakingly slow, and it can be difficult to locate the genes that have been mutated. The *piggyBac* transposon, when injected into fertilized mouse eggs along with an enzyme called transposase, is remarkably efficient at inserting itself into important coding regions of the genome, and as its name implies, it carries genetic tags that allow researchers to locate mutations quickly.

Moreover, *piggyBac* has the added feature of total reversibility, which should allow scientists to verify that particular mutations have particular effects. In the presence of transposase, *piggyBac* easily hops into genes, and it remains in place in any offspring in subsequent generations that do not inherit the enzyme. But when these mice are mated with others who carry the transposase gene, *piggyBac* hops back out of genes without leaving a trace. These traits make *piggyBac* a "dream tool" for geneticists, Xu said. "This new technology will completely change the game of using mutagenesis to understand the function of mouse genes and, by extension, their human counterparts." *PiggyBac* could also be a promising new vehicle for human gene therapy, according to Xu, who said that, in addition to carrying tags, *piggyBac* can be engineered to carry new genes into the genome.

To demonstrate the potential of this genetic piggybacking, Xu and his colleagues used *piggyBac* to insert a gene for a protein that glows red under ultraviolet light into a mouse. However, many more experiments will be required to determine whether the transposon, or some variation of it, could reliably and safely transfer therapeutic genes to humans.

Xu's immediate goal is to use *piggyBac* to inactivate every gene in the mouse, one by one, a project that would be unthinkable with traditional mutagenesis methods. "For the past two decades, it has routinely taken about a year to mutate one gene in a mouse, and altogether about 3,000 genes have been knocked out in mice, out of a total of about 25,000 that are in the genome," Xu explained. With the help of *piggyBac*, he said, "in three months, with two students, we have done 75 genes."

—Pat McCaffrey



USING LASERS TO DETERMINE CELL FUNCTION

Through genetic tweaking, researchers at the School of Medicine have made fruit flies walk, jump and fly on command—by flashing a light at them. The scientists inserted rat ion channels into nerve cells that control flies' escape movements, then injected the flies with a chemical that would activate the ion channels when exposed to light. Gero A. Miesenböck, M.D., associate professor of cell biology at the medical school, who led the study that appeared in the journal *Cell* in April, said that the research offers a new way to learn how nerve cells govern behavior.

A livestock virus may offer a new approach to treating glioblastoma

Viruses are hijackers, wreaking infectious havoc by taking over a cell's machinery and using it to replicate. But their wily ways may not be all bad. Yale professor of neurosurgery Anthony van den Pol, PH.D., is harnessing their destructive power to develop a novel treatment for glioblastoma, the most common and aggressive form of brain cancer.

Glioblastoma strikes about 7,000 Americans each year, and most patients live just a year after diagnosis. Although it can be treated with surgery, radiation and chemotherapy, said van den Pol, the cancer usually comes back.

The idea of unleashing viruses to destroy tumor cells is beginning to gain validity, not just for brain cancers but also for ovarian, prostate and other kinds of tumors. When this line of research began two decades ago, scientists feared that the viruses would spread to healthy cells, so they genetically altered them to prevent them from replicating. But those inactivated viruses kill relatively few brain tumor cells. The Yale team hypothesized that a replicating virus would be much more effective.

Van den Pol and his colleagues bred several generations of vesicular stomatitis virus on glioblastoma cells, selecting for strains with the highest tumor-killing capacity. Then they tested the virus and saved those strains that did not infect normal cells. In a study published in the *Journal of Virology* in May, the researchers reported that the strain they developed selectively killed glioblastoma cells *in vitro*, and was able to infect and kill whole tumors in mice.

The results are promising, but van den Pol stressed that they are still preliminary. The team plans to expose the virus to different types of cells found in the brain to make sure that it will not infect them. "This is a highrisk strategy," he said, "but we're dealing with a disease for which at present there is no cure."

—Alla Katsnelson



et cetera ...

NEW TARGET FOR MELANOMA

Using a technology devised at Yale five years ago, researchers have found what may be a new target for treatment of melanoma. The Yale team used AQUA (automated quantitative analysis) to measure protein expression in melanoma tissue microarrays. In a study in *Nature* in July they reported that microphthalmiaassociated transcription factor (MITF), a protein involved in cell survival, abnormally copies itself many times over. This overexpression was prevalent in metastatic disease and correlated with decreased rates of patient survival.

This suggests, said David L. Rimm, M.D., PH.D., HS '93, an author of the study and associate professor in the Department of Pathology, that MITF may represent a distinct class of oncogene that is necessary for tumor progression. Reduction of MITF activity sensitizes melanoma cells to chemotherapeutic agents, and targeting MITF in combination with other drugs may offer a new approach to treating melanoma. —John Curtis

A TOLL ON INFECTIONS

In 1997 the late Charles A. Janeway Jr., M.D., and Ruslan M. Medzhitov, PH.D., professor of immunobiology, discovered *toll*-like receptors, or TLRs, molecules that alert the body's acquired immune system to the presence of microbial or viral invaders.

Scientists have since identified over a dozen types of TLRs, which detect proteins in bacteria and viruses but not those in the eukaryotic cells that make up our bodies. Some pathogens, however, are also eukaryotes, and a team at Yale and the National Institutes of Health wondered whether TLRs could recognize them.

In the June 10 issue of the journal *Science*, the group reported that TLR11, discovered in mice at Yale last year, triggers an immune response after it detects a protein in the virus that causes toxoplasmosis.

Team member Sankar Ghosh, PH.D., professor of immunobiology, said that while it is not yet clear whether humans have a functional version of TLR11, these studies should lead to development of novel strategies to combat these infections.

—Peter Farley

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Cardiologist Harlan Krumholz has published a handbook that he hopes will encourage patients to be involved in their treatment for heart disease.

Guiding patients through heart disease

A cardiologist provides a handbook so patients can better understand their disease and how to treat it.

Half of all patients don't take the medications that their doctors prescribe. And the majority of cardiac patients leaving the hospital don't know the target numbers for optimal blood pressure or cholesterol. For cardiologist Harlan M. Krumholz, M.D., M.SC., the Harold J. Hines Jr. Professor of Internal Medicine and of Epidemiology and Public Health, these findings reflect lost opportunities for patients to participate in their care. Hopes of fostering better patient involvement in their care motivated Krumholz to write *The Expert Guide to Beating Heart Disease: What You Absolutely Must Know* (HarperResource, \$14.95).

Krumholz said that patients who understand their disease and the options for treating it can collaborate more effectively with their physicians in choosing and following the strategies that are most likely to help them reach their goals. "If patients understand the rationale behind the strategies, they're more likely to follow them." Krumholz also argued that informed patients are more likely to get good care.

"We have this illusion that medicine is being practiced uniformly and is of high quality throughout the country," he said. "That perception is just not true. There is ample evidence that treatment strategies that are well-established by the literature and endorsed by national guidelines are not uniformly being recommended by doctors or pursued by patients."

Unfortunately, patients are not often encouraged to become well-educated about their condition, said Krumholz. "We're still in an era when most people come in, they're told what to do and given a prescription, and if they don't comply, they're seen as letting down the physician."

Patients seeking to educate themselves about heart disease may feel overwhelmed, however. "If you got sick, where would you start? There's such an avalanche of information," said Krumholz. He views his 152-page book as a "travel guide" that provides essential facts about how heart disease develops and what can be done to treat it. The book describes seven key strategies: controlling blood pressure, managing cholesterol, exercising, maintaining a healthy weight, managing blood sugar, quitting smoking and using medication effectively.

BOOK NOTES

For more on the book, visit www.expertheartguide.com





Attention Deficit Enter Disorder



Krumholz chose these seven strategies based on national guidelines and his expertise in evaluating the quality of heart disease care. A prolific researcher himself, he has helped set national standards for cardiovascular care for organizations ranging from the American College of Cardiology to the Department of Defense. Based on the published evidence, his book describes approaches that work (such as taking beta-blockers after a heart attack or controlling cholesterol with statins), those that probably help (eating fish regularly), those of uncertain value (taking vitamins) and those that have proven harmful (hormone replacement therapy for women).

A grant from the John A. Hartford Foundation in New York allowed Krumholz to hire a researcher—Susan Cheng, M.D., then a medical student at McMaster University in Ontario, now a resident in internal medicine at Johns Hopkins. Krumholz and Cheng field-tested the book: they sent about 100 copies to relatives, friends, friends of friends with heart disease and patients, asking them to circle sections that were confusing and to pencil in questions.

"We said, 'Write all over this. It won't hurt our feelings.'" Their approach seems to have worked; a critic for *Kirkus Reviews* writes that "Dr. Krumholz has a gift for translating jargon into clear, accessible language that the concerned reader can easily absorb."

Writing for a general audience was a departure for Krumholz. He has clinical responsibilities one day each week, and as director of the Robert Wood Johnson Clinical Scholars Program at Yale, he spends a lot of his time guiding postdoctoral fellows in the program as they do research on improving clinical care and population health. His own research appears in 40 to 50 articles annually. But he called those papers "just a means to an end."

"At the end of the day, it's not about the number of publications but about whether people can benefit from the work we've done. The book is a tool to help promote that."

—*Cathy Shufro*

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

Nanoscale Technology in Biological Systems

by Ralph S. Greco, M.D. '68, HS '73, et al. (CRC Press) This book presents the latest information on the interface between nanotechnology and biology, examining the principles underlying the application of nanotechnology to basic science research, applied research and clinical practice.

Songs From the Black Chair: A Memoir of Mental Interiors

by Charles Barber, M.H.A., associate of the Yale Program for Recovery and Community Health (University of Nebraska Press) In his account of working with homeless mentally ill patients in New York, Barber tells their tales of prison, AIDS, heroin, crack and sexual abuse and of the voices that plague them.

The Craft of Psychodynamic Psychotherapy

by Angelica Kaner, PH.D., assistant clinical professor in psychiatry, and Ernst Prelinger, PH.D., clinical professor of psychology and psychiatry (Jason Aronson) Clinical vignettes illustrate the fundamentals of psychodynamic theory and technique, tackling questions such as: What is psychotherapy? How long will it take? How does change happen?

Information Systems Research: Relevant Theory and Informed Practice

edited by Bonnie Kaplan, PH.D., lecturer in anesthesiology (medical informatics), et al. (Springer) This volume is organized in seven sections, with 33 full research papers providing reviews on the Information Systems (IS) discipline. It also includes papers featuring critical interpretive studies, action research, theoretical perspectives on IS research and the methods and politics of IS development.

Attention Deficit Disorder: The Unfocused Mind in Children and Adults

by Thomas E. Brown, PH.D., assistant clinical professor of psychiatry (Yale University Press) Drawing on recent findings in neuroscience and a variety of case histories from his own clinical practice, Brown defines Attention Deficit Disorder, describes how to recognize it in people of different ages and discusses how it can best be treated.

Heart Care for Life: How to Develop the Long-Term Personal Program That Works Best for You

by Barry L. Zaret, M.D., the Robert W. Berliner Professor of Medicine and professor of radiology, and Genell Subak-Sharpe, M.S. (Yale University Press) The authors outline the constants for the full range of cardiovascular conditions, from angina and heart attacks to high blood pressure and cardiac arrhythmias. They then guide readers through the process of assessing personal variables in order to develop an individual treatment and lifestyle program.

Emotional Comfort: The Gift of Your Inner Guide

by Judith M. Davis, M.D. '63 (Wilder Press) This book provides a self-hypnotic technique for attaining emotional comfort. According to Davis, the technique helps its practitioners to resolve chronic difficulties and to handle new ones that may arise.

Books & Ideas BOOK NOTES



Multiple Sclerosis as a Neuronal Disease

by Stephen G. Waxman, PH.D., M.D., professor of neurology, pharmacology and neurobiology (Elsevier Academic Press) This illustrated book brings together the latest information from clinical, pathological, imaging, molecular and pharmacological realms to explore the neurobiology of multiple sclerosis.

One Nation Under Therapy: How the Helping Culture Is Eroding Self-Reliance

by Sally L. Satel, M.D., HS '88, lecturer in psychiatry, and Christina Hoff Sommers (St. Martin's Press) The authors believe that talking about problems is no substitute for confronting them. They argue that "therapism" and the "trauma industry" have begun to undermine the self-reliance and fortitude that Americans have traditionally valued.

Physicians' Cancer Chemotherapy Drug Manual 2005

by Edward Chu, M.D., professor of medicine (oncology) and pharmacology, and Vincent T. DeVita Jr., M.D., HS '66, the Amy and Joseph Perella Professor of Medicine (Jones and Bartlett Publishers) Completely revised for 2005, this handbook is a guide to all aspects of cancer chemotherapy, including a catalog of over 100 drugs commonly used in cancer treatment.

Bone Regeneration and Repair: Biology and Clinical Applications edited by Jay R. Lieberman, M.D., and Gary E. Friedlaender, M.D., Hs '74, the Wayne O. Southwick Professor of Orthopaedics and Rehabilitation (Humana Press) This collection of articles by leading orthopaedic and craniofacial surgeons and researchers reviews the biology of bone formation and repair and the basic science of autologous bone graft, allograft, bone substitutes and growth factors, and explores the clinical application of this knowledge to patients with bone repair problems.

(IRE INDEADING)

The Cadaver's Ball: A Novel of Revenge

by Charles Atkins, M.D., lecturer in psychiatry (St. Martin's Minotaur) Atkins creates characters with a range of motivations in this psychological thriller of the lives and loves of three medical school friends.

The Lobotomist: A Maverick Medical Genius and His Tragic Quest to Rid the World of Mental Illness

by Jack El-Hai (Wiley Publishers) In the early 1940s, lobotomy was the last resort in an attempt to relieve intractable psychiatric symptoms. This type of surgery was first performed in the United States in 1936 by neurologist Walter J. Freeman, M.D., who received his undergraduate degree from Yale in 1916, and neurosurgeon James W. Watts, M.D.—who helped pave the way for psychosurgery by conducting research on chimps at the Laboratory of Primate Physiology at Yale. The practice, now discredited. continued for more than 40 years.

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

IN CIRCULATION

Personal librarians help students navigate research

Second-year medical student Kurtland Ma ran into a snag while doing research last summer in Hong Kong: he couldn't download an article on alternative HIV therapies that he'd found online. Luckily, Ma had someone to turn to—his "personal librarian" 8,000 miles away in New Haven.

That librarian was Lynn H. Sette, M.L.S., a reference librarian and one of 10 librarians at the Cushing/Whitney Medical Library paired with students in medicine, in the Physician Associate Program and in the Combined Program in the Biological and Biomedical Sciences. Just as Sette had introduced herself to Ma during his medical school orientation, each of the personal librarians meets new students as they arrive, establishing librarian-student partnerships.

When Ma sought help from Sette via e-mail in July, she sent him the article he needed. Normally, said Ma, he does well on his own. "I've done so many PubMed/Ovid searches in the past and the website is so good that I don't feel like I need all that much help—having a personal librarian seems more like a luxury," Ma wrote by e-mail from Hong Kong. "I obviously didn't expect to be asking for her help from here in Hong Kong, but now I'm starting to realize that having her is quite helpful."

Education Services Librarian Jan Glover, M.L.S., who helped create the program nine years ago, said students often turn to their librarians when they begin third-year clinical rotations. They ask for guidance—in person or by e-mail—when they're looking for "the perfect bit of information to answer a clinical question." Students also ask for help with technical problems such as downloading a medication database onto a personal digital assistant.

The most common questions are about complicated literature searches. During the past year, third-year medical student Argo P. Caminis estimated that she has asked Glover for advice two or three times a week while doing research for two journal articles on adolescent sexual behavior. Glover showed Caminis how to avoid being inundated by thousands of citations on a broad topic.

"I was getting tons of hits. She helped me to focus it by the types of journals I was looking at: whether they'd been peer-reviewed, looking for literature review articles, limiting the search to recent or relevant articles. She taught me principles of research that I think were helpful to learn early on in medical school," said Caminis, who was a co-author on an article published last spring and who will be lead author on a second. "It's a good way to reach out to students." —Cathy Shufro

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

ON CAMPUS



DOUGLAS MELTON In the stem cell debate, asking the right question

The intertwined debate that links abortion to embryonic stem cell research has revolved around the wrong question, said Douglas A. Melton, PH.D., co-director of the Harvard Stem Cell Institute. "I would suggest to you," he said in his keynote address at the annual meeting in May of the Associates of the Cushing/Whitney Medical Library, "that the question of when does life begin is the wrong question. The real question is: 'When does personhood begin?''

A sperm and an egg are already alive before they meet, Melton said, rendering the notion of the beginning of life an arbitrary matter of timing. When does personhood emerge? "This is a metaphysical question that everyone should think about."

Harnessing the plasticity of stem cells and inducing their differentiation into a desired tissue is years away, Melton said, but within reach. "I predict the 21st century will be a century not about genes and DNA, but about cells and stem cell research. ... Genes are not the unit of life. Cells are the unit of life."

—John Curtis



PHILLIP SHARP A new role for RNA as a regulatory molecule

In the last few years scientists have been surprised by small nucleotide sequences, microRNAs and siRNAs (small interfering RNAs), that appear to play a role in both suppressing and promoting cancer. "We are at a transition in our understanding of RNA," said Phillip A. Sharp, PH.D., Nobel laureate and Institute Professor at the Massachusetts Institute of Technology. "RNA is taking on a new role. It is a regulatory molecule."

These small RNAs are doublestranded sequences of about 22 nucleotides that act by disrupting messenger RNA. According to Sharp, they regulate up to a fifth of human genes, a function once thought to be the exclusive province of proteins. "The double strand is the signature key that converts the RNA into a regulatory molecule," Sharp said in June as he gave the Adelberg Lecture sponsored by the Department of Genetics.

This regulatory role could have therapeutic value if it can be harnessed to turn off mutant, disease-causing genes. "The big problem with using siRNAs is how to introduce them into the cell," Sharp said. "That delivery problem stands between this being a very broad platform for therapeutics and where we are at now."

—J.C.



GLORIA STEINEM Research that makes women visible

Surveying a packed ballroom at New Haven's Omni Hotel in which women were disproportionately and diversely represented, renowned feminist author and activist Gloria Steinem noted the changes since she first spoke at Yale at the dawn of the women's movement in the 1960s. "The phrase gender-specific could have applied to all of Yale," Steinem said in April. "And God and Man at Yale has at least become God and People. There are glorious racial and ethnic and economic differences and diversity and richness. So times have really changed."

Speaking at a gala event in which she received a Women of Vision award from Women's Health Research at Yale (WHRY), Steinem lauded the work of WHRY, which supports research on sex-specific factors in health and disease. "Their questions at a time when mostly old answers rule the top are really very, very crucial," she said. "The rock-solid research that is going on makes the female half of the world visible and is clearly something we all desperately, desperately need right now."

—Peter Farley



JOSHUA STEINERMAN Fuggedaboutit! Transient Global Amnesia

A 62-year-old man led a choir through a flawless rehearsal and performance, but by the end of the day he could remember none of the day's events.

He was experiencing transient global amnesia (TGA), a malady believed until the 1950s to be the product of hysteria or malingering, said Joshua R. Steinerman, M.D., a senior resident in neurology who described the disorder at clinical neuroscience grand rounds in June.

Physicians now know what triggers TGA, without knowing what causes it. Triggers include swimming in cold water, sexual intercourse, an emotional event, stress and exertion. "The history and proximal events leading to the episode are crucial," Steinerman said.

Episodes usually last four to six hours. Sufferers—typically people between the ages of 50 and 79—know something's wrong, but they can't recall answers to the questions they ask as they try to orient themselves.

Over the years, several theories have been proposed about what causes TGA. "None is entirely satisfactory," Steinerman said. "The great thinkers who proposed mechanisms have always hedged their bets." —J.C. 16

From the Middle East, in the Middle Ages

An exhibit at the Sterling Memorial Library highlights the contributions to medicine of Muslim physicians.

By Jennifer Kaylin





When we check into a hospital, take our children to the pediatrician or undergo a surgical procedure, it's likely we're benefiting from the work of medieval Muslim doctors and scholars.

"Muslims' Contributions to Medieval Medicine and Pharmacology," an exhibit of manuscripts from the Medical Historical collection at the Harvey Cushing/John Hay Whitney Medical Library, was on display in Sterling Memorial Library's exhibit corridor until September. The exhibit, said Simon Samoeil, curator of Sterling's Near East Collection, was designed to "provide positive insight" into the important contributions made by medieval Muslims at a time of high tensions between our nation and areas of the Muslim world.

In the seventh century, when former empires such as those of the Greeks, Persians and Romans fell under Arab domain, the new Islamic empire inherited many scholarly disciplines, including the developing fields of medicine and pharmacology. Recognizing their importance, Islamic leaders had works from other languages translated into Arabic, so research and study could continue.

The exhibit includes some remarkable examples of these early texts, including an illustrated Persian treatise on human anatomy, with six pages of detailed drawings. There is also a human anatomy book that was translated from Greek into Arabic by the 11th-century scholar and physician Avicenna. "His textbook was used in the West until the mid-17th century," Samoeil said.

Other artifacts in the exhibit include a medical dictionary and a book containing 31 chapters of practical information about hygiene, sexual intercourse and other topics. These Arabic translations of Greek scholarship led to later translations into Latin, Samoeil says, paving the way for Greek knowledge to become accessible to the scientists and scholars of the Renaissance. In addition to these important translations, Muslims introduced new fields of medical research and clinical practice, including gynecology, embryology and a focus on the care of mothers and children. Samoeil said medieval Muslims saw the larger value in protecting the health of women. "Women are the mothers of men," he said. "If the Arab empire was to flourish, the women needed to be healthy."

Early Arabs also contributed to the diagnosis, treatment and prevention of diseases such as smallpox and measles, and Muslim doctors were the first to incorporate surgery, then a separate discipline, into the study of medicine and to develop its practice and techniques.

Perhaps the most concrete legacy is the structure of today's hospitals, which follow the model of ninthcentury Islamic hospitals. These early health care centers had open admission policies for patients of all economic backgrounds, regardless of sex, religion or ethnicity. They were run by a large administrative staff and organized into wards by gender and nature of illness. In addition, early Islamic hospitals pioneered the idea of having on-site pharmacies and training programs for students to get practical experience under the guidance of a physician.

Samoeil said the exhibit drew a favorable response from the Yale community and visitors. "The other day, I overheard three tourists," he said. "One called out to another, 'Come look at this. It's amazing. I didn't know the Arabs and the Muslims had done all this.' "

His goal in organizing the exhibit, he said, was to draw connections between the past and the present. "It's important to do that," he said. "When we look at modern materials and manuscripts, it's important to understand how we got there, to see the connection with what came before."

Jennifer Kaylin is a contributing editor of *Yale Medicine*.

OPPOSITE TOP The 11th-century Persian manuscript *Farah namah* was also known as *Ajayib al-dunya* (*Wonders of the World*). Multicolored illustrations of animals, birds, plants, stones and humans adorn the text.

OPPOSITE BOTTOM The 11th-century scholar and physician Avicenna wrote a medical text that was used until the mid-17th century. **BELOW** The *Kitab al-Hawi*, believed to have been written in the 9th or 10th century, was still in use in the 1600s, when the Shah of Iran ordered it copied for his chief physician. The page shown below describes the structure of the brain as well as ailments that afflict it.

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In January 2004 Johnnie Yates, M.D. '95, took a job as a physician in an international clinic in Kathmandu, the capital of Nepal. The post offered a chance for Yates to pursue his interests in travel medicine, and as he recounts in the article that follows, a typical day in his life provided insights into medicine in Nepal.

LETTER FROM KATHMANDU

Article and photographs by Johnnie Yates, M.D. '95





OPPOSITE On the path to the base camp of the world's highest peak.

BELOW During his 18 months in Nepal, medical school alumnus Johnnie Yates took frequent trips to mountain locations, such as Poon Hill in the Annapurna Himalaya.

The rain starts innocently with scattered sprinkles—warning enough for street vendors to cover their wares and for pedestrians to seek cover. The sky darkens and the downpour begins. Rain pounding on the roof can make a telephone conversation next to impossible. And then it stops. "Must be the beginning of the monsoon," I presume, but I learn that June is too early. Once the monsoon season (July to September) starts in earnest, the rain becomes a daily occurrence and provides relief from the heat and humidity.

Premonsoon rains herald the end of the spring trekking season, and work at the CIWEC Clinic Travel Medicine Center in Kathmandu, Nepal, slows down. CIWEC stands for Canadian International Water and Energy Consultants, the nongovernmental organization (NGO) that established the clinic in 1982. It has since become an independent center staffed by three physicians (a U.S.trained Nepali internist, who is also the medical director, and two American doctors). CIWEC is internationally renowned for its Western standard of care and its research into the health problems of foreigners. Most patients are diplomats, staff from development agencies and NGOS, aid workers, volunteers and tourists. During busy periods the waiting room resembles a mini-United Nations, with British diplomats, Tibetan monks, Israeli backpackers and American parents and their newly adopted Nepali children awaiting consultations. Trekkers and climbers felled by altitude sickness come to the clinic as well.

I never imagined living in Nepal, a landlocked country between India and China. Apart from reading Jon Krakauer's *Into Thin Air*, about the 1996 Mt. Everest climbing disaster, or listening to Bob Seger's version of "Kathmandu," I never thought about the place. I graduated from medical school in 1995, completed a residency in family practice at Middlesex Hospital in Connecticut, and was living in Hawaii when I received the unexpected offer to work at CIWEC. I had done medical school electives and volunteer work abroad but always preferred the tropics to the mountains. Nonetheless, the opportunity allowed me to pursue my interest in travel medicine full time. So in January 2004, I packed away my "aloha" shirts, dusted off my cold-weather clothing and moved to Nepal.

Slightly smaller than New England, Nepal has a population of approximately 25 million, with over 1.5 million people living in Kathmandu. It is best known as home to Mt. Everest, at 29,035 feet the world's highest mountain, but its lowland tropics offer a chance to go on safari in search of rhinos and tigers. The latter part of the dry season (February to May) is a popular time to visit the country, especially for trekkers and climbers.

On that rainy day in June, my first patient was Shyam, a 4¹/₂-year-old Nepali boy adopted a week earlier by an Italian couple. His cheeks had become swollen and painful over the past few days and he refused to eat. 19



Trekkers hike in the shadow of Mt. Ama Dablam, a 6,856-meter peak in the Khumbu region of Nepal, along a popular route to Mt. Everest Base Camp.



Both of his parotid glands (salivary glands below the ears) were swollen and tender, and he was mildly dehydrated. He also had scabies and a scalp infection, conditions present in nearly all of the children that I see from orphanages. Shyam's new parents said the orphanage had no proof of any vaccinations, thus increasing my clinical suspicion of mumps.

For a country in which the burden of infectious disease is high, diagnostic capabilities can be woefully limited. While some medical technology has reached Nepal, it does not mean that a system of modern health care delivery has come along with it. One night I had to obtain a CT scan of a patient with fever, convulsions and delirium (ultimately diagnosed as encephalopathy due to typhoid fever). After an initial noncontrast CT at the university teaching hospital, the radiologist inquired if I wanted one with contrast, which would highlight an abscess. Upon my affirmative reply, he scribbled on a scrap of paper. Sensing my confusion, he explained that I would have to take the note to the pharmacy down the street, buy the contrast agent and bring it back for him to administer.

Shyam was stoic, even as an IV was inserted to provide hydration. I wondered what was going through his mind. He had spent most of his young life in an orphanage before he was taken away by a friendly foreign couple he could not understand. Did he realize that in one week he would board an airplane for the first time and fly to his new home in Italy?

After I finished caring for Shyam, I called for the next patient. There was no answer from the waiting room. At CIWEC, that means that the patient is in the bathroom. Diarrheal illness accounts for a third of what we see, and the incidence increases between May and July. Regardless of how careful one is, the pathogens that cause diarrhea are impossible to avoid—I realized this after being stricken five times in my first two months in Nepal.

Bacteria are responsible for most of the diarrhea among foreigners in Nepal. However, the premonsoon season ushers in the seasonal parasite *Cyclospora cayetanensis*, which causes cyclosporiasis, a debilitating diarrheal disease characterized by marked fatigue and anorexia and first identified in Nepal in 1989 by a CIWEC lab technician.

The patient emerged from the bathroom with a big sigh and recounted how he had had intermittent diarrhea for two weeks. Every time he thought he was recovering, the diarrhea would return. He had no energy or appetite and was losing weight. His stool examination confirmed *Cyclospora*. He was treated with trimethoprim/ sulfamethoxazole and reassured that his appetite should improve within a few days. Untreated, cyclosporiasis is self-limiting, but it can last up to several weeks.

After lunch Mr. Sherpa, a 40-yearold Nepali, presented with four days of fever and headache. His symptoms put typhoid at the top of the list of possible diagnoses. However, Sherpa had recently returned from the West

Swayambhunath, a center of Buddhist thought on a hill overlooking Kathmandu, is also known as the "monkey temple," because of the wild monkeys that live nearby.

Bengal region of India, an area endemic for malaria. A blood smear revealed severe *Plasmodium falciparum* malaria, the most dangerous of the disease's four forms. I started an IV, administered an antimalarial and transferred him to the hospital for closer monitoring. In Kathmandu one can lose valuable time while waiting for an ambulance, so Sherpa was sent to the hospital by the quickest means available—a taxi.

As it turned out, Sherpa's ride to the hospital was held up by political demonstrations in the streets. What should have been a 15-minute ride took nearly an hour. Nepal has become increasingly plagued by political problems: an eight-year-old Maoist insurgency and a Maoist-imposed blockade of the Kathmandu valley in August 2004 made international headlines. Political parties calling for a return to a democratically elected government (dissolved by the king in 2002) frequently stage demonstrations and call for strikes. In addition to delaying patient transport, the protests can directly affect a patient's health as well-on one occasion police threw tear gas into a hospital because political agitators had fled there.

Later in the afternoon a frantic call came from Mrs. Paddington, whose husband worked for a British development agency. Her 4-year-old daughter Daisy had stuck a bead deep into her right nostril. Daisy was more preoccupied with the toys in the waiting room than the commotion that her action had caused. After a few unsuccessful attempts at blowing the bead out (by pinching off the opposite nostril and exhaling into the child's mouth, a task assigned to Daisy's mother), I used forceps to retrieve a *bean*, rather than a bead. Mom had no idea where the bean came from, and Daisy denied putting anything up her nose. After a scolding from mom and a sticker from the nurse, she skipped happily out of the clinic. I then headed home on my bicycle.

It takes me about 15 minutes to ride home. I live in a quiet residential neighborhood a few blocks from the prime minister's residence. On the rare days when the air is unpolluted and the skies are crystal clear, I can see the Himalayas from the second floor of my house. The traffic in Kathmandu is a tangle of bicycles, motorcycles, tempos (local three-wheeled transport), cars and buses, all negotiating the congested streets. Vehicles swerve and stop without warning to avoid oblivious pedestrians, crater-like potholes and sacred cows (literally-Nepal is a predominantly Hindu country). The chaotic traffic combined with the noxious pollution frequently tests my patience, and one day I found myself laughing after I realized I had "road rage" from riding my bicycle.

As I reached my doorstep, the telephone rang. A British volunteer called to say she had been attacked by several monkeys while walking near a temple. The attack was unprovoked and, interestingly, the woman's two friends were unmolested. She had several scratches on her legs and was frightened about contracting rabies. Rabies is endemic in Nepal and monkeys are potential reservoirs. Because she had not been immunized, she required human rabies immune globulin along with a series of five vaccinations over four weeks.



"Not your typical day back home," I mused. However, as I thought about what I had seen that day, something was bothering me. Most of the problems were preventable-mumps is rare in the United States due to routine immunizations; better sanitation and a safe water supply would prevent much of the diarrhea in Nepal; Sherpa would not have contracted malaria had he taken prophylaxis; and the volunteer's risk of rabies and her anxiety about it would have been alleviated had she been vaccinated prior to coming to Nepal. As for the bean in the nose ... well, I've seen that back home and I suppose there's no way to curb a child's curiosity. YM

Johnnie Yates, M.D. '95, recently took a position with Kaiser Permanente at a clinic on Oahu.

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A soldier covers his head while another remains alert during on August 2004 battle with Shiite militias in the holy city of Najaf.

The unseen JOUIDES of war

As long as humans have waged war, the horrors of the battlefield have caused psychological damage. Since the war in Vietnam, this damage has had a new name post-traumatic stress disorder.

by Cathy Shufro

Il but one of the 12 veterans sitting around the plastic laminate conference table appear worn and tired. Their world-weary look comes from decades in which, among them, they shot heroin, smoked and drank too much, wasted years in jail, picked fights, gambled, divorced and shuttled from job to job. They all fought in Vietnam, and more than 30 years later, as they enter their late 50s and early 60s, they are still paying the price.

Except for Luke. The former Marine is only 24 years old, 18 months back from Iraq, and he looks good. Blond, fit and handsome, he could model for a recruiting poster. But he has joined the other veterans in a United Way meeting room in Meriden, Conn., because he is hurting, too. If someone yells at him, he'll yell back, or worse. If someone steps into his bedroom, he'll smell the alien scent hours later. If someone touches him when he's sleeping, he'll attack. Thunderstorms scare him. In the months after returning from war, he went to bars, got drunk and picked fights with strangers nearly every day.

Luke provides a sense of purpose for the other vets. Guided by 57-year-old social worker and Vietnam veteran James J. Gavin, M.S.W., the older men talk about their own problems over coffee and doughnuts this morning. All, including the social worker, have been diagnosed with posttraumatic stress disorder (PTSD). For these men, the psychological and physiological adaptations that helped them to survive war persisted at home. Veterans traumatized by war-or people distressed by an event in which they fear death or great harm to themselves or others-suffer from PTSD if they meet three criteria: re-experiencing, hyperarousal and avoidance. That is, people with the disorder unwillingly revisit traumatic events in flashbacks or nightmares; they are hypervigilant, feeling irritable about trivial frustrations, constantly scanning a room or a street for danger, seeming to sleep with one eye open; and they retreat from life and

relationships because they feel emotionally numb or because they hope to avoid situations that trigger bad memories.

Gavin has helped the Vietnam veterans at the table to understand, after all these years, that they have not been messing up their lives simply because they have bad memories of Vietnam, but rather because their brains have been changed by war. The changes that helped them to survive Vietnam have made their lives back home a kind of purgatory, from the aisles of Stop & Shop to the family dinner table. The men generally took decades to realize that they had PTSD.

Gavin recognized that Luke had PTSD shortly after Luke came home in July 2003 after five months in Iraq. They met when Luke stopped by the Vet Center in West Haven, Conn., a community center sponsored by the Department of Veterans Affairs (VA), to ask about college money. During several conversations about benefits, Gavin tried to assess whether Luke had PTSD. He already knew from his Vietnam experience that many veterans come home with PTSD; a landmark study in 1988 showed that one in three men who served in Vietnam would experience PTSD. Gavin saw it in Luke and persuaded him to join the therapy group in the winter of 2004.

One of the men explains why he is glad Luke is among them. "It helps us share our experience dealing with this for 30 or more years," says Vincent, a slight man with gold-rimmed glasses and curly black hair who looks like a professor and spent a year in a homeless shelter. "Luke has the advantage of all this wealth of understanding. We didn't have any of this."

They talk mostly about feeling rage. Joe tells his story first. His huge, muscular arms are covered with many-colored tattoos, and he wears a T-shirt that reads: "When it absolutely, positively, has to be destroyed overnight: U.S. Marines." He describes the time that an elderly woman banged her supermarket shopping cart into his. Once. Twice. The third time,



James Gavin was diagnosed with post-traumatic stress disorder after fighting in Vietnam. Now a social worker, he leads other veterans in discussions of their problems.

Joe overturned the woman's cart and kicked her groceries across the floor. After security guards ejected him from the store, he rushed to his car and drove away. "I felt terrible. This poor lady just ran into me a few times."

"You can't help it," explains Craig, a mild-mannered man wearing glasses and a red sweatshirt. Vincent adds: "You have a sense of being attacked."

"You wake up one day and you're out of toothpaste, and you want to nuke the whole neighborhood," says Bob. He says that driving brings out anger in all the men at the table. But nowadays, says Bob, he stays a bit calmer when other drivers cut him off on the highway. "I've gotten better," he says with a wry smile. "I don't chase them to their doorsteps any more."

Luke is making progress, too, even though he went to the emergency room recently after he became angry at his brother and slammed his fist through a door.

"You're doing better," Gavin tells him. "Six months ago you would have hit *him*."

The 12 men around the table speak of rage and regret, of wasted years. But toward each other, they express compassion. With Gavin's help, these men are going to take care of Luke.

A malady with roots in ancient times

The deep psychological wounds of war have been documented since the time of Homer in ancient Greece. His account of the Trojan War tells of Achilles' disintegration following the battlefield death of his best friend. The psychological impact of war was called "nostalgia" during the Civil War and "shell shock" in World War I. But it was not until 1980 that the military and medical establishments in the United States formally recognized the damage done by combat stress. The age-old psychiatric illness is now called PTSD.

A Yale psychiatrist was one of the first clinicians in the nation to recognize a distinctive set of symptoms related to the Vietnam War. Arthur S. Blank Jr., м.D., нs '65, who practices psychoanalysis and psychiatry in Bethesda, Md., had spent a year in Vietnam working in hospitals in Long Binh and Saigon after finishing his Yale psychiatry residency. Soon after the war ended, Blank reviewed the charts of 60 Vietnam veterans and concluded that many had been misdiagnosed with maladies ranging from alcoholism to schizophrenia. Blank invited those men to a therapy group at the veterans hospital in West Haven, Conn., now called the VA Connecticut Healthcare System. That was in 1973, the year that most of the remaining American soldiers came home from Vietnam; the PTSD diagnosis would not be included in the American Psychiatric Association's diagnostic manual for seven more years.

"Very early on, West Haven became a center where they really understood PTSD," says Steven M. Southwick, M.D., HS '85, professor of psychiatry, who does research at the West



Psychiatrist Steven Southwick studies the neurobiology of stress responses.

Haven VA hospital. Other clinicians nationwide also began to notice the distinctive effects of war trauma that Blank had observed, and by the late 1970s, mental health professionals united to push for the official definition of PTSD.

Soon after, Yale endocrinologist John W. Mason, M.D., now professor emeritus of psychiatry, showed that the behavioral changes of PTSD had neurobiological correlates. Combat veterans with PTSD had elevated levels of stress hormones such as noradrenaline and adrenaline.

"This was a giant step," says Southwick, "because people began to understand that there was a biological basis to many of the 'psychological responses' they were seeing in people who were severely traumatized."

Since then, Yale investigators at the VA have remained at the center of PTSD research and have helped improve the care of returning veterans nationally; West Haven is home to the Clinical Neurosciences Division of the VA National Center for PTSD, whose other divisions are located in Massachusetts, Vermont, California and Hawaii. Yale researchers have found that veterans with PTSD not only undergo changes in stress hormone levels but may also have hyperreactive sympathetic nervous systems; exaggerated increases in heart rate and blood pressure; and reductions in the volume of the hippocampal region of the brain, which is critical for memory and learning.

Yale researchers are studying the neurobiology of PTSD from several vantage points. John H. Krystal, M.D. '84, FW '88, the Robert L. McNeil Jr. Professor of Clinical Pharmacology, is working with Robert A. Rosenheck, M.D., HS '77, professor of psychiatry, to study whether the antipsychotic medication risperidone helps veterans who don't respond to antidepressants like Prozac and Zoloft. Krystal is planning to investigate whether genetic factors influence how people respond to these antidepressants. C. Andrew Morgan III, M.D., associate clinical professor of psychiatry, has worked with the military to study how military personnel respond to severe stress. He found that personnel who responded best to stress had elevated levels of neuropeptide Y, a brain chemical linked to stress.

Southwick, who is deputy director of the Clinical Neurosciences Division of the national VA PTSD center, is taking part in another PTSD study. The study is a collaboration with Deane E. Aikins, PH.D., assistant professor of psychiatry, and Maj. Paul M. Morrissey, M.D., FW '00, HS '02, a psychiatrist and chief of behavioral health at Fort Drum in upstate New York. Using functional MRI scans, they are charting variations in brain function between controls and veterans diagnosed with PTSD. Southwick says that studying the neurobiology of stress responses—and finding a physical manifestation of a psychological problem—had helped clinicians to understand PTSD better. "Before, it was all interpreted psychologically," he says.

Depression and an adrenaline rush

Since October 2001, more than 1.1 million men and women have served in Iraq and Afghanistan, according to the Department of Defense. A research team at the Walter Reed Army Institute of Research reported in the July 1, 2004, issue of *The New England Journal of Medicine* that nearly one in six Iraq veterans and one in nine Afghanistan veterans suffered from PTSD, major depression or generalized anxiety.

Such studies provide the best window into PTSD rates, because according to Defense Department physician Michael E. Kilpatrick, M.D., "the Department of Defense would only know of those service members who reported problems and sought a diagnosis." And many do not report their distress: in the Walter Reed study, between 60 and 77 percent of the study participants who had a mental disorder did not seek help.

The most exposed of those fighting in Iraq and Afghanistan may be members of the Reserve and National Guard, which make up 35 percent of those deployed, notes Morgan. They are vulnerable, he says, because Reservists and National Guard members generally have less training than do full-time troops. He notes that the high rate of redeployment in the wars in Iraq and Afghanistan hurts morale and increases burnout; by last summer, 280,000 of the I.I million had gone back, according to the Department of Defense.

Blank agrees that redeployment can intensify harm: returning for a second tour worsened PTSD for troops who served in Vietnam. "There's some evidence that it has something to do with addiction to the adrenaline rush, which may have a physical as well as an emotional component." (As one Connecticut veteran of Iraq described it, "Nothing can compare to it when you come home. Everything is boring. You can't but be drawn into that intensity. Everyone I've talked to feels the same way.") The effects of trauma can last a long time. The congressionally mandated Research Triangle Institute study in 1988 that compared 1,625 Vietnam veterans with 750 other veterans and 750 civilian counterparts found that 15 years after the war's end, 15 percent of male veterans and 9 percent of female veterans were suffering from PTSD. This compares to a rate of about 1 percent of the general population.

For those fighting in Iraq and Afghanistan, Blank predicts that the changing character of the wars will increase the rates of psychological trauma. "Unfortunately the situation in both combat zones is one of general terror," says Blank. "There are no safe places, and as the guerrilla fighters know all too well, it's highly psychologically debilitating to have random terror." Blank notes that anecdotal reports suggest that at least some troops think the war is unjustified, and for those men and women "the questionable character of the war in all likelihood will contribute to the occurrence of PTSD, because there is not the buffering factor of feeling that despite the difficulties one has encountered, there is at least a sturdy justification for what one has experienced."

Blank points out one "good-news aspect" of the situation: Reservists and National Guard members tend to be older than full-time service members, and age protects against PTSD. The most vulnerable to the disorder are 18- and 19-year-olds. Another positive aspect is that now veterans can get care much more quickly than did Vietnam vets. But the majority of veterans have historically shunned care. They avoid it in part because society stigmatizes people with PTSD, says Blank, who helped to establish and then directed the VA network of Vet Centers like the one that employs Gavin. The communitybased counseling centers now number 206 nationwide.

Military officials are working against the stigma, according to Fort Drum's Morrissey. He says that troops leave for war knowing that psychological distress is normal and that, even in a war zone, the military will provide support. That's a big change from the military's approach during the Vietnam War.

"The main thing that's changed is that now the possibility of combat stress and other mental health problems, including PTSD, is mentioned up front," says Morrissey. He says that this kind of openness is helpful, because men and women anticipating combat inevitably worry about what will happen if they fall apart. They ask themselves: "'What if I am really scared? What if I lose it when I'm there?' They're all thinking about this stuff," says Morrissey. He and his staff train soldiers how to recognize problems not only in oneself but also in others. "If they can be looking out for someone else, that helps them regain some mastery." Making it clear that those with problems will get support, says Morrissey, "lets them push themselves a little further."

Those who do have trouble coping can seek help from "combat stress control teams." Stationed in the war zones, the teams are composed mostly of mental health specialists



Social worker Susan Hill helps veterans with their re-entry to civilian life.

who have completed basic training and then spent eight months studying emergency medicine and mental health care. They are backed by psychologists, psychiatrists and social workers. The combat stress control teams offer those in distress a short break and medication, if necessary. Once symptoms are mitigated, the service members return to their posts. As Luke describes it, the goal of a battlefield psychiatric evaluation is to find out: "Are you fit to pull the trigger?"

Finding help at home

Once home, veterans can seek help at a VA hospital or a VA Vet Center, says Dolores Vojvoda, M.D., assistant professor of psychiatry at the medical school and head of the PTSD and anxiety disorder service at the West Haven VA. Vojvoda says some veterans are referred by VA physicians but most call the VA for help on their own. The West Haven staff includes five part-time psychiatrists, a psychologist, three social workers, a registered nurse and three advanced-practice mental health nurses.

Vojvoda reported that by mid-summer, therapists in the PTSD clinic at the West Haven VA hospital had seen about 50 Iraq and Afghanistan veterans. She expected the numbers to grow, and the VA had recently awarded Vojvoda's group a grant to hire a new psychiatrist and two more social workers in anticipation of an influx of combatants returning with PTSD and anxiety disorders.

The VA staff provides both individual and group therapy. In the groups, veterans learn about the symptoms of PTSD and how to manage them. Treatment may also include antidepressants, sleeping pills, antipsychotic medication for intrusive memories and anger, and alpha blockers for nightmares and exaggerated startle reflex. The VA also offers programs to help veterans recover from alcohol and drug abuse, common mechanisms for coping with PTSD.

Group and individual therapists at VA hospitals often treat patients using cognitive processing therapy, a technique developed in the 1980s for rape survivors. Patients are asked to focus on a traumatic event and to examine whether they have interpreted it realistically. For instance, a soldier may take the blame for a bad event, but the idea of fault implies some control over what happened. In reality, he or she may have been powerless to prevent what happened. The therapy also addresses overgeneralizations, such as when a person harmed by another concludes that no one can be trusted.

Therapists counseling returning service members face a paradox because so many returnees must go back to war. Susan R. Hill, M.S.W., assistant clinical professor of psychiatry (social work) at the medical school and a social worker at the West Haven VA hospital, worries about helping those with PTSD relax their vigilance if they are to be returned to a combat zone where they will once again need to be hypervigilant. "It's a really questionable outcome at the moment for the ones going back."

Joining a group is difficult for those with PTSD, since avoidance and withdrawal are hallmarks of the disorder. Nonetheless, says Hill, "We are convinced that there's tremendous benefit in being around folks who are dealing with re-entry." She notes that many veterans withdraw from other people, "and then they're pretty much isolated in their own heads, as we all are when we are alone, only their heads are full of carnage. … The opportunity to speak with other people who are having trouble with re-entry breaks down the military 'strong-men-dor't-cry' theory."

Luke, for one, is doing better. "You learn when you are in danger of getting set off, and you learn to avoid any kind of stress, any situation where you're going to get set off," he says.

At the restaurant where he works as a cook, the boss yells at other employees—but not at Luke. "I told him when I got hired: 'You can't yell at me.' "

He told his girlfriend: "If I hit you in my sleep, I'm really sorry. If I hit you hard, I'm really, really sorry. If I'm screaming, get out quick." So far the two have co-existed peacefully in bed.

Although he finished his military service more than two years ago, Luke still toys with the idea of going back to war. He is attracted by "the rush that was associated with it. When things start going bad here, I think, 'The hell with it, I'll go back.'"

Instead, Luke has enrolled in college. He wants to emulate James Gavin and become a social worker. "I look at the way I was before I met Jimmy and how much better I am now, and I think it's a rewarding job to help somebody with what they're going through. ... He's been through the same shit I've been through, and he was my age when he did. He was in a bad place, and he pulled himself out. Now he's helping other people." YM

Cathy Shufro is a contributing editor of Yale Medicine.







Breaking the back of polio

In the 1940s, Yale's Dorothy Horstmann solved a puzzle that would lead to the first polio vaccines 50 years ago this year.

by David M. Oshinsky, PH.D.

Fifty years ago this year, following the largest public health trial in American history, a killed-virus polio vaccine developed by Jonas Salk, M.D., was found to be safe, potent and effective. The news set off a national celebration. Salk became an instant hero, the country's first celebrity-scientist, a miracle worker in a starched white lab coat. But as the years passed, the essential contributions of other researchers to this lifesaving vaccine were lost to history. Dozens of men and women had been involved—at Harvard and Yale, at Johns Hopkins and the Rockefeller Institute for Medical Research, at the University of Michigan, the University of Pittsburgh and the University of Cincinnati. What follows is the story of Dorothy Millicent Horstmann, M.D., FW '43,

Patients stricken with the most severe form of polio were confined to iron lungs, such as those seen in this ward at Haynes Memorial Hospital in Boston in August 1955. **ABOVE** Dorothy Horstmann, in her laboratory in the 1970s, was the first woman to become a full professor at the medical school. The national trial of the Salk polio vaccine began in 1954, when Richard Mulvaney gave an injection to Randy Kerr at Franklin Sherman Elementary School in McLean, Va.

whose patience and intuition produced a stunning breakthrough that made polio vaccines possible.

The story begins in June 1916, with a health crisis in Pigtown, a densely populated immigrant neighborhood of Brooklyn, N.Y. Frightened Italian parents had approached local doctors and priests, according to news accounts, "complaining that their child could not hold a bottle or that the leg seemed limp." When the first deaths followed a few days later, health department investigators rushed to Pigtown for a house-tohouse inspection. All signs pointed to a disease known as infantile paralysis, or poliomyelitis (soon shortened to "polio" by the newspapers to save headline space). As it spread from Brooklyn, communities across the Northeast closed their doors to outsiders, using heavily armed policemen to patrol the train stations and the roads. The epidemic, which lasted through October 1916, claimed 6,000 lives and left 27,000 people paralyzed. New York City alone reported 8,900 cases and 2,400 deaths, 80 percent of the fatalities being children under 5. There had been minor polio outbreaks in previous years, but nothing like this.

"The menace for the future," warned a federal health official, "is very real."

Polio is an intestinal infection spread by contact with fecal waste. The virus enters the body through the mouth, travels down the digestive tract and is excreted in the stool. Usually the infection is slight, with minor symptoms. In a small number of cases—about one in 100—the virus invades the central nervous system, destroying the motor neurons that stimulate the muscle fibers to contract. At its worst, polio causes irreversible paralysis, most often in the legs. Most deaths occur when the breathing muscles are immobilized, a condition known as bulbar polio, in which the brain stem is badly damaged.

Though poliovirus has long been present in the environment, the disease, unlike smallpox or influenza, had triggered no major outbreaks around the world. Why it took root in Western nations, especially the United States, during the 20th century is still a matter of debate. Some researchers pointed to more careful reporting and better diagnostic techniques. Others noted the circulation of more virulent strains of poliovirus, capable of multiplying at a ferocious rate. Still others saw a correlation between the spread of polio and the ever-increasing standards of personal hygiene in the United States—people were less likely to come into contact with



poliovirus early in life when the infection is milder and maternal antibodies offer temporary protection. Put simply, America's antiseptic revolution brought risks as well as rewards.

A dread disease strikes at random

By mid-century, polio had become the nation's most feared disease. And with good reason. It hit without warning. It killed some victims and marked others for life, leaving behind vivid reminders for all to see: wheelchairs, crutches, leg braces and deformed limbs. In 1921, it paralyzed 39-year-old Franklin Delano Roosevelt, robust and athletic, with a long pedigree and a cherished family name. If a man like Roosevelt could be stricken, then no one was immune.

Each June in America, like clockwork, came newspaper photos of jam-packed polio wards and eerily deserted beaches. Newspapers ran tallies of the victims—age, sex, type of paralysis—akin to baseball box scores. Children were warned not to jump into puddles or share a friend's ice cream cone. Parents checked for every known symptom: a sore throat, a fever, the chills, nausea, an aching limb. Some gave their children a daily "polio test." Did the neck swivel? Did the toes wiggle? Could the chin reach the chest?

In truth, polio was never the raging epidemic portrayed by the media, not even at its height in the late 1940s and early 1950s. Ten times as many children would be killed in accidents in these years, and three times as many would die of cancer. What had changed following World War II was the incidence of polio in the United States as well as the rising age of the victims, a quarter of whom were now older than 10. From 1940 to 1944, reported polio cases doubled to eight per 100,000, doubled again to 16 per 100,000 between 1945 and 1949, and climbed to 25 per 100,000 from 1950 to 1954, before peaking at 37 per 100,000 in 1952. "The United States had never experienced a higher crest of the epidemiological wave," a journalist noted of the 57,000 reported cases that year, "and never would again."

The drive to combat polio was led by the National Foundation for Infantile Paralysis, now known as the March of Dimes. The genius of this foundation lay in its ability to single out polio for special attention, making it seem more ominous, and curable, than other diseases. Its strategy would revolutionize the way charities raised money and penetrated the world of medical research. Millions of foundation dollars would be spent to set up virology programs and polio units across the **BELOW** During World War II Horstmann traveled as a member of the Yale Poliomyelitis Study Unit to Hickory, N.C., site of one of the worst outbreaks in the 20th century. **RIGHT** The March of Dimes campaign allowed anyone to make a contribution. In the 1940s the campaign used a "dime card" for collections.



country, with the first grant going to the Yale School of Medicine in 1936. Although research funding went in many directions, one point became increasingly clear: the best way to prevent polio would come through a vaccine.

This was hardly a revelation. Vaccines already had proved successful against other viruses—smallpox and rabies being notable examples. But producing a safe and effective one against polio would not be easy. Three major problems had to be solved. First, researchers would have to determine how many different types of poliovirus there were. Second, they would have to develop a safe and steady supply of each virus type for use in a vaccine. Third, they would have to discover the true pathogenesis of polio—its route to the central nervous system—in order to fix the exact time and place for the vaccine to do its work.

The first problem took the longest to solve. Dozens of strains were examined, using the stools, throat cultures and, in fatal cases, nerve tissue of polio victims. Most of this work was done by ambitious young researchers hoping to attract March of Dimes grant money. (The list included Salk at the



University of Pittsburgh.) As it turned out, all of the 196 tested strains of poliovirus fit neatly into three distinct types. The poliovirus family proved remarkably, conveniently, small.

A polio vaccine, then, would have to protect against all three virus types to be successful. The next step involved the harvesting of poliovirus that was safe enough, and plentiful enough, for use in that vaccine. At Harvard, John F. Enders, PH.D., a Yale College graduate, Frederick C. Robbins, M.D., and Thomas H. Weller, M.D., using *in vitro* cultivation, grew poliovirus in non-nerve tissue—a breakthrough that would win them the Nobel Prize in physiology or medicine. By cultivating these viruses in a test tube, rather than in the brain or spinal column of a monkey, researchers could get a better look at the changes occurring in polio-infected cells. Far more important, a safe reservoir of poliovirus had now been created, free from the contaminating effects of animal nerve tissue. And that, in turn, made possible the mass production of a vaccine.

But a major problem remained to be solved. Though Albert B. Sabin, M.D., and others had speculated that poliovirus entered the body through the mouth and worked its way down the digestive tract, no one had yet discovered traces of the virus in the victim's bloodstream. How, then, did it wind up in the central nervous system? The answer would come from a research laboratory at Yale.

A girl's impossible dream in a world of men

Horstmann had a powerful fantasy as a child: she imagined herself as a doctor. Born in Spokane, Wash., in 1911, she grew up in San Francisco, where as a teenager she accompanied a physician friend of the family as he made his rounds through the local hospital. Earning her undergraduate (1936) and medical (1940) degrees from the University of California, San Francisco, Horstmann recalled that it had "never crossed my mind that [this] was in any way unusual for a woman. ... It was quite natural."

In 1941, Horstmann applied for a residency at Vanderbilt University Hospital in Nashville, where the chief of medicine, Hugh Morgan, M.D., had a strict policy of choosing only men. "I got back a polite letter, saying no," she recalled in an unpublished interview with historian Daniel J. Wilson, PH.D., of Muhlenberg College in Pennsylvania. "I wasn't exactly crushed, but I was disappointed." Six months later, while considering an offer to **BELOW** Celebrities joined in the campaign against polio. In 1954 actress Grace Kelly distributed March of Dimes literature to leaders of the Mothers' March on Polio.



enter private practice in San Francisco, she received a note from Morgan asking if "Dr. Horstmann" was still interested. She was, indeed. Somehow, Morgan had forgotten that Dr. Horstmann was a woman. Horstmann later learned from his secretary that when Morgan discovered his error, he "all but went into shock. ... But we became friends, and I had a very good year there."

When Horstmann subsequently applied for a postdoctoral fellowship at Yale, her first visit to New Haven did not go well. She had hoped to study with John R. Paul, M.D., a young pathologist who had co-founded the Yale Poliomyelitis Study Unit in 1931 with James D. Trask, м.D. As luck would have it, Paul had been called away to study a polio epidemic, leaving Horstmann to meet with Francis G. Blake, M.D., the acting dean. A giant in the field of infectious disease who was known to generations of medical students as "stuffy and remote," Blake couldn't quite picture Horstmann at Yale. Indeed, she recalled, he "went on to tell me how the last woman he had on the house staff did something awful." Offended, and blissfully ignorant of the dean's imposing reputation, she replied that "if a woman on the house staff did not live up to expectations it was remembered for the next 50 years, but if the person was a man, it was forgotten by the next year." Horstmann was told the decision would be up to Paul. "He accepted me," she said, "and that is how it all began."

In 1942, with World War II under way, she arrived at Yale. As head of the Commission on Neurotropic Virus Diseases of the Army Epidemiological Board, Paul was constantly traveling to remote parts of the world. Concentrating on the spread of polio among Allied troops in North Africa, Paul confirmed the theory that adults from areas with high sanitary standards, such as Western Europe and the United States, were far more susceptible to the disease than the local population, which had built up immunity following generations of exposure.

In New Haven, Horstmann joined the Yale polio unit. Missing its two founders—Trask died of a bacterial infection in 1942 while working at an Army camp—the ranks included a handful of superb researchers, such as Joseph L. Melnick, м.D., and Robert Ward, м.D. Using an approach pioneered by Paul and known as "clinical epidemiology," the polio unit, including Horstmann, tracked polio epidemics in Connecticut, Illinois, New Jersey, western New York state and Hickory, N.C., site of one of the worst outbreaks of the 20th century. The unit tested water and sewage, trapped flies and other insects and took blood samples from those who had the disease and those without symptoms, hoping to discover both the route of poliovirus through the body and the manner of transmission from one person to another. For Horstmann, who had come to Yale to study Streptococci, the switch to polio was inspiring. "It had a dramatic immediacy," she said. "When you deal with an epidemic you realize it's an urgent thing. There was so much to be learned."

Tracking polio's pathogenesis

Like others in the polio group, Horstmann combined her clinical studies with laboratory research. During a polio epidemic in New Haven in 1943, she collected blood specimens from every patient admitted to the hospital with symptoms of the disease—111 in all. Only one tested positive for poliovirus, a little girl with minor neck pain. Was it possible, Horstmann wondered, that poliovirus was only present in the bloodstream during the brief period before a victim took sick and the physical symptoms became apparent?

To test this theory, she began a series of experiments on monkeys, feeding them poliovirus by mouth to determine if, and when, it turned up in their blood. The results were dramatic. Poliovirus was detected within days of the feed**BELOW LEFT** Braces and the iron lung became symbols of the feared disease. The epidemic reached its peak in the early 1950s, climbing to 37 cases per 100,000 in 1952. **BELOW RIGHT** This 1953 cartoon offered simple instructions for avoiding poliovirus.

ings. Why had so many others failed to discover this? The answer was deceptively simple: they had waited too long before looking. Horstmann's discovery, published in 1952, would pave the way for both the Salk killed-virus polio vaccine and the Sabin live-virus polio vaccine.

Working independently at Johns Hopkins, researcher David Bodian, PH.D., M.D., later reported almost identical results. When poliovirus enters the blood, it creates the very antibodies that will soon destroy it, wiping away the signs of its existence. Horstmann had determined the time (early in the infection) and the place (the bloodstream) for the battle against polio to be waged. Her findings meant that an immunizing vaccine, packing low levels of antibody, could destroy the virus before it entered the central nervous system. In a personal letter to Horstmann in 1953, John F. Fulton, M.D., D.PHIL., Yale's distinguished historian of medicine, proclaimed: "This disclosure is as exciting as anything that has happened in the Yale Medical School since I first came here in 1930 and is a tremendous credit to your industry and scientific imagination. ... It is also medical history."

That history would continue. In 1959, the World Health Organization sent Horstmann to the Soviet Union, Czechoslovakia and Poland to evaluate the massive public health trial involving Sabin's oral polio vaccine. Her favorable report led the way to its licensing, and widespread acceptance, in the United States and beyond. Worldwide the incidence of polio fell to 1,919 cases in 2002, a decline of 99 percent since 1988, when 350,000 cases were reported. The United States has not seen a case of wild polio since 1979.

In later years, Horstmann became the first female professor of medicine at Yale (1961), the first woman in the university to hold an endowed chair (1969) and an elected member of the National Academy of Sciences (1975).

Horstmann died in 2001. Today her portrait hangs at the School of Medicine in a gallery of luminaries from the 19th and early 20th centuries. She is the only woman honored on these walls. **YM**

David M. Oshinsky, PH.D., the George Littlefield Professor of American History, University of Texas at Austin, is the author of *Polio, An American Story: The Crusade That Mobilized the Nation Against the 20th Century's Most Feared Disease*, published this year by Oxford University Press.







Dean Robert Alpern has spent his first year at Yale getting to know the medical school and bringing the faculty together in a strategic planning process.
A year at the helm

Since he arrived at Yale in 2004, Dean Robert Alpern has led faculty to a new vision of the medical school, with a focus on clinical expansion and the application of great science.

By Michael Fitzsousa

It's 8 a.m. on a Wednesday morning in late July, and Robert J. Alpern, M.D., has assembled his senior leadership group for its weekly meeting. About halfway through today's agenda, the five people at the table are discussing options for an electronic medical record, or EMR. The computer-based patient chart is becoming a must-have in medicine's transition to the digital age. Computerized record-keeping lessens the likelihood of a mistake being made—preventing a medication from being prescribed at a dangerous dosage, for example, or ordered for an allergic patient. It also holds promise for clinical researchers hunting for patterns in the illnesses, interventions and outcomes of patients, to determine which treatments work best for which groups of individuals.

The problem is that the medical school and its affiliated practice and hospitals do not yet share an EMR or a data repository, the computerized warehouse where data from medical visits, tests and surgical procedures are stored. There are competing software products, a still-shifting technology platform, major costs to implement and maintain a system and many questions remaining about how to get doctors to adapt to new ways of charting patient information and ordering drugs and tests. A central dilemma, Alpern notes, lies in the trade-off between ease of use and specificity: the systems that are most practical for physicians are the least useful for researchers, while those that standardize data entry in a way that makes sense for research are unwieldy for busy doctors.

This issue is just one of eight or nine broached at today's weekly meeting, unusual in that the agenda is fairly short. Some weeks it grows to as many as 25 or 30 items, all of which need to be moved forward during the three-hour session. Today's topics include the potential reorganization of one of the academic departments, planning for a new center for clinical research, two or three new fund-raising opportunities, a review of the medical school's website, the retreat for department chairs in the fall, a proposal for a student-run free clinic and renovations to the school's day care facility. Alpern, a nephrologist and Ensign Professor of Medicine, moves things along but allows the discussion to meander enough to pull in many points of view. From time to time, he takes an index card out of his shirt pocket and jots down a few words on the back of his schedule for the day.

The talk eventually leads to the perennial space crunch at the medical school and the constant juggling of lab, office, clinical and teaching space inherent in managing a growing institution of 1,787 full-time faculty members, 1,150 students and more than 3,000 full-time employees. Two years ago the 457,000-square-foot Anlyan Center opened on Congress Avenue, and a new, smaller building on Amistad Street is almost complete, but still there is not enough room for new programs and people. Space is at such a premium that Alpern holds a weekly meeting to work on the ever-changing puzzle. "Everything is so dependent on facilities, and you view but is enough of a pragmatist to know that a higher ranking will help the school attract the best faculty and students.

He also has two giant tasks ahead of him: leveraging Yale's formidable strength in the basic sciences to translate knowledge about molecules and cells into new ways of treating illness, and putting those treatments to work in a much larger patient base. Yale has long been known as a powerhouse in biological science but has not had the same scope

"Everything is so dependent on facilities, and you always have to think years in advance. I still think we're one building away from where we need to go."

always have to think years in advance," he says. "I still think we're one building away from where we need to go."

Before the discussion draws to a close, Alpern excuses himself to take a call, a rare interruption of the weekly meeting. As it turns out, the occasion is anything but ordinary: a successor to Joseph Zaccagnino, M.P.H. '70, the president and CEO of Yale-New Haven Hospital (YNHH, the school's primary teaching hospital and clinical partner), has been named and will be announced later in the day.

Opportunity in New Haven

Alpern came to Yale the summer before last from the University of Texas Southwestern Medical Center. Dallas is a world away from New Haven in its geography, politics, culture and climate, but it shares a rich tradition in science with the medical school. It was a young Yale medical graduate, Donald W. Seldin, M.D. '43, HS '46, who transformed the Southwestern campus from a compound of Quonset huts in the 1950s to the powerhouse in basic science and medical research that it has become. Alfred G. Gilman, M.D., PH.D., the Nobelist who succeeded Alpern as dean there, is a Yale College alumnus and son of one of the Yale pharmacologists who developed the first chemotherapy treatment for cancer in the 1940s.

Alpern was recruited to Yale not only to lead a worldclass medical school with an annual budget of more than \$750 million, but also to counter several unsettling trends, including a mounting operating deficit (\$35 million in fiscal 2004) and a general perception that the school was beginning to slip in relation to some of its peers. Third in funding to medical schools from the National Institutes of Health in 1993, the school still brings in more than \$260 million in federal grants, but gradually dropped to eighth place during the 1990s and early 2000s as other schools were expanding their campuses and research capacities. Its ranking in the U.S. News & World Report annual survey of research medical schools dropped from third in 1996 to 11th this past June. Many academicians dismiss the rankings, arguing they lack scientific rigor and rely too heavily on subjective assessments-reputation in particular. Alpern understands that

and depth in clinical practice, despite a handful of subspecialties that attract patients from outside the region, a few of them internationally. Alpern wants to expand the medical school's programs in cancer care, cardiovascular medicine, organ transplantation and other key areas of practice to raise Yale's profile nationally.

His honeymoon period as dean may still be in effect, but many faculty members are pleased by what he has done in his first year. Robert Udelsman, M.D., M.B.A, the Lampman Memorial Professor of Surgery and Oncology and chair of surgery, says Alpern is "available, approachable and affable, and he appears willing to delegate to others and empower them." With the appointment of a new hospital CEO—Marna P. Borgstrom, M.P.H. '79 (See *Chronicle*, p. 5)—and a new dean at roughly the same time, Udelsman says, the medical center is presented with an unusual opportunity.

"Here is the entrée for Yale-New Haven Medical Center to make a fundamental decision about what it wants to be, whether it wants to be the best [medical center] in the world—not just in the top 10, but number one," Udelsman says. "The hospital can't do it alone, and the medical school can't do it alone."

David L. Coleman, M.D., HS '80, the interim chair of the Department of Internal Medicine, says that Alpern worked hard during his first year on the school's relationship with YNHH, the recruitment of department chairs and the launching of a strategic planning process that occupied 70 faculty members on three committees from last December until August. Throughout the planning process, Alpern dropped in on meetings and participated in the discussion, helping guide it at times but mostly listening. "I would say the key word to my management style is consensus building," he says. "I don't try to force people to do things. I try to think things out so that I have a vision for where we should go, and then I try to build a consensus."

Planning for the future

Alpern sees the strategic planning effort, which was shared by three committees evaluating basic science, clinical practice and clinical and population-based research, as a major contribution to the healthy functioning of the medical school. (A fourth committee has been evaluating the educational mission in a separate process.) "Two of the best things that have come out of it are communication and the creation of a common sense that the institution has a direction," he said in an interview in late summer, as the final reports were being circulated among the planning groups and edited into final form. "In a university, you have each faculty member marching to the beat of tive and convenient for patients without dampening the entrepreneurial spirit that has driven progress in the specialties and subspecialties.

"The faculty at Yale in general are all excellent doctors, but in many cases we don't have enough of them to provide good service to our local and more national constituency. In addition, we don't have the mechanisms in place to provide such service," Alpern says. Patients should be able, with

"We need to become a very user-friendly medical center that patients can navigate easily and where they can uniformly receive the highest level of care."

his or her own drummer, and if you get the best faculty, that works. But an institution should also have a sense of direction, and people felt we didn't."

Among the recommendations to come out of the planning process was the establishment of large multidisciplinary programs in stem cell biology, cardiovascular medicine, cancer, genetics and the neurosciences. The planners also identified areas of infrastructure that needed strengthening, as well as strategic "cores," or pooled resources, to provide the latest technology and expertise to faculty conducting research. One example, discussed at the dean's group meeting, is a center for clinical and population-based investigation bringing together the statisticians, study designers, computer scientists, regulatory professionals and others who are essential to the conduct of large studies evaluating new drugs and medical procedures.

From the basic science committee, the dean received recommendations for expanding or starting academic programs as well as bolstering certain portions of the academic infrastructure. For example, the group urged expansion of the Combined Program in the Biological and Biomedical Sciences (which has unified graduate education across the medical school and central campuses) and investment in animal facilities, X-ray diffraction equipment for structural biologists, laboratories for drug development and testing, small-molecule screening systems, RNAi screening (a hot technology that promises to identify potential new drug targets many times more quickly than previous methods) and advanced biomedical imaging.

The clinical committee focused on even more basic infrastructure: mechanisms for improved planning, communications, marketing and support services, as well as an EMR and a central scheduling service to standardize the way appointments are made. Like many medical schools, Yale saw its clinical departments grow quickly in the 1970s, '80s and '90s with an autonomy that would surprise many outsiders. For years, each ran its own ship and handled its own scheduling and administrative operations. Now the challenge is to make sure the system as a whole works in a way that is effecease, to make appointments, schedule tests, obtain results, see multiple specialists and count on good communication among them and their referring physicians—things that cannot always be taken for granted, Alpern says. "We need to become a very user-friendly medical center that patients can navigate easily and where they can uniformly receive the highest level of care."

That task has been entrusted to David J. Leffell, M.D., HS '86, the newly appointed deputy dean for clinical affairs, who has been the driving force behind the 750-member Yale Medical Group since 1996. Other members of the senior leadership team are Jaclyne W. Boyden, M.B.A., the deputy dean for finance and administration; Carolyn W. Slayman, PH.D., the deputy dean for academic and scientific affairs; Martha E. Schall, M.B.A., the university's associate vice president for development and director of medical development and alumni affairs; Mary J. Hu, M.B.A., the director of planning and communications; and Julie B. Carter, J.D., an associate general counsel of the university.

Alpern cites the formation of the leadership group as one of the most important accomplishments of the past year. The group provides a structure for dealing with the complex problems the medical school must deal with, the EMR being just one example from this week's meeting. "The problem is, it could be very easy. We could go real fast and do it wrong," he says of the EMR process. To make good decisions, Alpern does what most corporate CEOS would do and works closely with a small group of senior leaders in whom he has complete confidence, delegating authority to them. There is a twist, however.

"Most people would tell you that you should have no more than about six direct reports, and unfortunately, that's where the system breaks down in academics," he says. Such a business model would have the 27 academic departments reporting to one of the deputy deans, but Alpern says, "I couldn't stand that model. It removes the dean from the academic presence of the medical school, and it would frustrate any good chair. Plus it would take me out of what I consider some of the most enjoyable parts of the job." Instead, Alpern meets weekly with his core group and at least biweekly with the department chairs. If something comes up, he adds, "any chair can get on my calendar within a week." A newly formed dean's advisory group of senior faculty will assist in major decisions affecting the school. In addition, Alpern has scheduled regular meetings with the departmental faculty so that he visits with each department once a year. know is that you're a professor. I really believe all the tracks are equal."

Teaching is also of critical importance to the school's future, and Alpern says Yale has one of the best educational programs in the world. "The Yale System, I think, is great, in that it allows the students to focus on learning rather than on grades and to explore their own unique interests through the thesis. It's just terrific. It's how you create the leaders of tomorrow."

If the bottom line drove every decision and no investments were made, it would be a disaster.

A long commute

Alpern is married to nephrology researcher Patricia A. Preisig, M.S., PH.D., who remained in Dallas for the first year of his deanship, while their daughter, Rachelle, finished high school (she entered Yale as a freshman this September, and their son, Kyle, is a sophomore at the Hopkins School in New Haven). Alpern spent the first year commuting home on the weekends to Dallas, where he held his weekly lab meeting he moved his nephrology lab to Yale in August—and took up tennis again after many years, joined by his son. Originally from Long Island, N.Y., where his parents and his sister and her family still live, Alpern says he was happy at Southwestern but was attracted both by the opportunity to come to Yale because of its position as a leading medical school and by the chance to help solve its problems.

"I wouldn't have moved for a school that wasn't as good as Yale," he says, "and I'm not sure I would have come if it was not a chance to really put my fingerprint on Yale."

He sees empowering the clinical faculty as one of the most important tasks before him. He and Leffell speak daily about clinical issues and have put a great deal of effort into building up the Yale Cancer Center (more than a dozen cancer clinicians have been recruited in the past year), relaunching the school's liver transplant program and placing faculty who are primarily clinicians on an equal footing with their counterparts in research. Getting promoted at a top medical school traditionally has hinged on prowess in the lab, for scientists and clinicians alike, but in recent years Yale and some of its peer institutions have introduced new faculty tracks that reward clinical excellence. Last year, Yale lifted its cap on the number of faculty in one of these categories, the clinician-educator track, because Alpern felt the clinical practice could not grow otherwise. "I told the provost, there's no choice here. We must lift this cap, and [then-Provost] Susan Hockfield said okay," he says. "Anyone who's really an outstanding clinician and educator who has a national reputation will be promoted to professor. And when you're a professor here, your title doesn't say what track you're on. All people

Alpern says the least pleasant parts of the dean's job are the schedule—he has meetings from 8 a.m. to 7 p.m. most days, is out several evenings a week, answers e-mail late into the night and works through the weekends—and getting and dealing with bad news. For example? "Faculty who want to leave," he says. "That's probably the most unpleasant and the most important to deal with. When you have a great faculty, they're constantly under attack" by competing schools wanting to recruit them. He is also under pressure to balance the budget while making major investments in the school's future. Those two goals might seem contradictory, but Alpern says they go hand in hand. Cost containment is a critical piece of the equation, and so are fund-raising and a policy of well-thought-out expansion. If the bottom line drove every decision and no investments were made, he says, it would be a disaster.

Encouraged by his first year, Alpern says he has no doubt the school will reach its goals. From his perspective, the good days in the dean's office outnumber the bad days by a wide margin. "I'd say the proportion is about 10 to 1, good days to bad," he says.

Is he serious about that ratio? Well, yes, Alpern says, while acknowledging the extreme sunniness of the estimate. "You have to understand, I'm an optimist," he adds. "You can't ignore some of the bad news, but I try to focus on the good things." **VM**

Michael Fitzsousa is the editor of Yale Medicine.

OB HAMBLY

A half-century of change

RECORDS

A retired pathologist looks back on 50 years of evolution in medicine and what it means for the future.

Reminiscing about the world of medicine my colleagues and I entered 50 years ago is like flipping through old *Life* magazines. Not only has everything changed, but the rate of change continues to accelerate. I have seen these changes in my work as a laboratory director at an inner-city teaching hospital, where I have been responsible since the early 1960s for introducing new technologies. I have also been an ambivalent witness to the extraordinary transformation of the landscape in health care delivery.

My first clinical laboratory was really an extension of those encountered in college premedical programs. There were guinea pigs, frogs and rabbits for microbiology. Photometers were just replacing the human eye for evaluating the color changes in chemical reactions. Of the 40 tests we offered, we had done about half as medical students. Fast forward: like most middle-size hospitals, mine now offers more than 2,000 diagnostic tests, with 375 done in-house. Analytical systems are automated, from order entry to printing charts. Units of measure have shifted from grams to picograms or parts per billion. The original "big three" studies in radiologythe chest film, gall bladder series and barium enema—have been replaced by MRIS, PET and CT scans.

When I graduated from Yale in 1956 the physician-patient relationship was usually one-on-one. House calls were common. There were eight medical specialties. Physicians generally knew all 20 or so major drugs. Office records were kept on 5-by-7 cards, and \$3 in cash covered an office visit. My original malpractice bill for \$100,000 per incident/\$300,000 per year was \$24. Bureaucracy and paperwork were minimal and overhead expenses negligible. Insurance companies paid fees without hassle, and the clinician had autonomy to make medical decisions.

By the '6os and '7os massive expenditures in research began to generate new knowledge, new technologies and sometimes unrealistic expectations. Younger, procedure-oriented subspecialists were riding the crest of the wave. However, the bulk of physicians, mostly older generalists, were less fortunate. Many found themselves caught in a tangle of double-digit overhead expenses, fixed reimbursement schedules, new mandates, audits, benchmarks, business models in which patients are "customers," electronic records, "keeping up" and gloves-off competition for patients. By the late '80s, for some clinicians, compensatory mechanisms that had allowed them to maintain the status quo began to break down, sweeping away the lives they had known. Once unthinkable, "denying access" became a reality. Symptoms of "burnout" were growing. Some clinicians have retired early. Some, though disgruntled, plod on. Others have, for the first time, become active politically, especially to effect tort reform. Many physicians warn students not to go into medicine!

The two great forces that changed our professional lives—new knowledge and limited resources—will have an even greater impact on those now entering the system. Consider this: The best estimates are that, worldwide, \$90 billion annually is being spent on research and development in the biological sciences—producing some 8,500 articles per day! And with the national debt growing and with the fiscal integrity of Social Security, Medicare and Medicaid threatened, massive increases in health care funding are unlikely. These two forces will keep the lives of young physicians in perpetual turbulence.

Yet I do not see the future of medicine as bleak. The core mission of medicine, enunciated throughout the ages, endures. The basic needs of the human race are not changing. What will continue to change are the technology and the organizational framework, including financing, by which the potential of this technology will be made available to society as a whole. Fortunately those entering the system are already developing the necessary survival skills: they know they must keep learning and adapting, and they have expectations attuned to the current system. Some will come to understand the need to get active politically. They will not be caught unprepared, as our generation was, for the rapid transformation of health care. They enter the profession expecting change.

Dwight F. Miller, M.D. '56, HS '58, is an associate clinical professor of pathology at the School of Medicine.

WE WELCOME SUBMISSIONS

Do you have an opinion to share on a vital topic in medicine, health or science? Send your thoughts to Essay, *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612, or via e-mail to ymm@yale.edu.



Gail D'Onofrio

D'Onofrio named head of emergency medicine

GAIL D'ONOFRIO, M.S., M.D., associate professor of surgery (emergency medicine), has been named section chief of emergency medicine at the medical school and chief of adult emergency services at Yale-New Haven Hospital. She had led both services in an interim position since 2004.

D'Onofrio practiced nursing for many years before getting her medical degree in 1987. She chose emergency medicine, she said, for the excitement of making a radical difference in patients' lives, literally in seconds. She calls her practice one of "controlled chaos" and acknowledges that it takes a particular personality to cope. In addition to her clinical work, she has done research on using the emergency department to move alcohol and drug abusers into treatment. She recently received a \$3.6 million grant from the National Institute on Alcohol Abuse and Alcoholism to test a counseling intervention with harmful and hazardous drinkers. Half of all major traumas are alcohol- or drug-related, so addressing substance abuse can prevent visits to the emergency department.

In her dual roles she manages emergency departments on-site and at a satellite clinic in Guilford, Conn., and conducts research, teaches medical students and is responsible for emergency physicians in residency. She is also medical director of Women's Heart Advantage, a New Haven-based program aimed at educating patients and clinicians about the risks of cardiovascular disease in women. And she heads Project ASSERT, a program in which health promotion advocates screen emergency department patients for drug and alcohol abuse.



Carolyn Slayman

Fund honors a mentor, boosts young scientists

When Applera Corp. of Norwalk, Conn., asked members of its board of directors last spring to suggest recipients for gifts from the company, CAROLYN W. SLAYMAN, PH.D., the medical school's deputy dean for academic and scientific affairs and a member of Applera's board, suggested a grant that would also promote her ideals in biomedical education.

Slayman earmarked \$300,000 to endow a fund that will support Yale's Combined Program in the **Biological and Biomedical Sciences** (BBS) and honor the memory of her mentor and thesis advisor, Edward L. Tatum, PH.D. She met Tatum at Rockefeller University in New York City, where she earned her doctorate under his supervision in 1963, a few years after he won the Nobel Prize in physiology or medicine for pioneering work on genetic regulation of metabolism in the cell. "For a very famous man—he was at the height of his career—he nonetheless took extraordinary measures to work closely with every student and every postdoc in his lab group,"

recalled Slayman, Sterling Professor of Genetics and professor of cellular and molecular physiology.

Tatum, who died in 1975, did part of the research that led to the Nobel while he was on the Yale faculty. Tatum and his graduate student Joshua Lederberg, PH.D. '47, who shared the prize, along with Harvard geneticist George Wells Beadle, PH.D., discerned how bacteria exchange and recombine genetic material, findings that paved the way for gene sequencing and genetic engineering.

Ever the scientist, Slayman said she hopes the Applera gift will be "autocatalytic"—a term from chemistry for the mechanism by which the products of a reaction provide fuel for further reactions—and will inspire others to support the BBS program. Applera's contribution already shows signs of self-replication: it stands to benefit from a university policy that matches endowment gifts to the School of Medicine, which will double its impact.

Applera is the parent company of Applied Biosystems, which develops and markets scientific equipment, and Celera, which played a major role in sequencing the human genome.



Edward Tatum



Edward Zigler

Center renamed in honor of "father" of Head Start

At a celebration in July, the Yale Bush Center in Child Development and Social Policy was renamed in honor of EDWARD F. ZIGLER, PH.D., Sterling Professor Emeritus of Psychology, considered the "father" of the Head Start program. Zigler was also the founder of the center, now called the Edward Zigler Center in Child Development and Social Policy.

The center is one of the nation's oldest centers for child and family policy research. It has been part of the Department of Psychology and the Child Study Center, where it serves a critical role in training and scholarly research.

Walter S. Gilliam, PH.D., assistant professor at the Yale Child Study Center, who has been affiliated with the Zigler Center since 1995 and is known for his studies of state-funded prekindergarten systems, has been named director of the center. Matia Finn-Stevenson, PH.D., will remain as associate director, and Sandra J. Bishop-Josef, PH.D., will continue as assistant director. Zigler will serve as director emeritus.

Zigler is regarded as the nation's leading researcher of programs and policies for children and families, having planned or implemented such national programs as Head Start, Early Head Start and the innovative School of the 21st Century. Founded by Zigler in 1978 with funding from the Bush Foundation of Minnesota, the center works to improve the lives of America's children and families by bringing the results of empirical research on child development into the policy arena.



Henry Binder



Alison Galvani



Theodore Holford Akiko Iwasaki

Glenn Micalizio

Lynne Regan







Sandra Resnick

Raymond Yesner

Sandra L. Alfano, PHARM.D., an associate research scientist in the department of medicine, has been appointed chair of one of the medical school's two institutional review boards for research involving human subjects. As chair of Human Investigation Committee I, Alfano is responsible for overseeing several hundred research protocol applications a year.

Roland E. Baron, D.D.S., PH.D., professor of orthopaedics and rehabilitation and of cell biology, received the D. Harold Copp Award from the International Bone and Mineral Society in June, for "outstanding achievements in basic research in the fields of bone and mineral metabolism that have led to significant changes in understanding of physiology or disease."

Henry J. Binder, M.D., professor of medicine (gastroenterology) and of cellular and molecular physiology, received the 2005 **Distinguished Achievement** Award from the American Gastroenterological Association in May. The award honors his research into the pathophysiology and treatment of diarrheal diseases.

Joyce A. Cramer, B.S., associate research scientist in psychiatry, was elected in May to the board of directors of the International Society for Pharmacoeconomics and Outcomes Research, an organization dedicated to translating research into practices that lead to efficient and equitable allocation of scarce health care resources.

Stanley J. Dudrick, M.D., professor of surgery (gastroenterology), received the 2005 Jacobson Innovation Award from the American College of Surgeons in June. He was honored for his contributions to science, medicine and education through his research and achievements in nutritional support for surgical patients. In 1967 Dudrick demonstrated that infants could receive nutrition intravenously and still grow and develop.

Alison P. Galvani, PH.D., assistant professor of epidemiology (microbial diseases), received a Young Investigators' Prize in June from the American Society of Naturalists for her work in evolutionary ecology.

Theodore R. Holford, PH.D. '72, the Susan Dwight Bliss Professor of Epidemiology and Public Health and head of the division of biostatistics, was elected a fellow of the American Statistical Association.

Akiko Iwasaki, PH.D., assistant professor of immunobiology, is one of 11 recipients of the 2005 **Burroughs Wellcome Fund** Investigator in Pathogenesis of Infectious Disease Award, which will allow her to study the role of mucosal lining cells in the initiation of immune responses against viral infections.

Becca R. Levy, PH.D., associate professor of epidemiology (chronic disease), has been named a fellow in the Behavioral and Social Sciences section of the Gerontological Society of America. Fellows are recognized by their peers for outstanding contributions to the field of gerontology.

Judith H. Lichtman, PH.D., M.P.H. '88, assistant professor of epidemiology (chronic disease), received the Women with Heart Research Award in June from the American Heart Association for her work on her research grant "Prospective Registry for the Predisposing Factors, Care and Outcomes of Myocardial Infarction in Young Women."

Glenn C. Micalizio, PH.D., assistant professor of chemistry, has been named a 2005 Beckman Young Investigator. The Young Investigator Awards are given annually by the Arnold and Mabel Beckman Foundation to support promising young faculty members in the early stages of their careers in the chemical and life sciences.

Linda M. Niccolai, PH.D., assistant professor of epidemiology (microbial diseases), received a three-year, \$240,000 grant from the Patrick and Catherine Weldon **Donaghue Medical Research** Foundation to examine sources of repeat chlamydia infections in young women. Niccolai's multidisciplinary study, which will continue through 2007, will provide a more complete understanding of the factors that influence the trajectory from initial diagnosis to repeat infection.

Lynne J. Regan, PH.D., professor of molecular biophysics and biochemistry and of chemistry, has won a fellowship from the John Simon Guggenheim Memorial Foundation for her studies of novel anticancer reagents.

Sandra G. Resnick, PH.D., assistant professor of psychiatry, received the 2005 U.S. Psychiatric Rehabilitation Association Carol T. Mowbray Early Career Research Award, one of five presented by the association for outstanding contributions to the field of psychosocial rehabilitation. Resnick is the associate director of the Northeast Program Evaluation Center of the Veterans Health Administration.

Steven M. Strittmatter, M.D., PH.D., the Vincent Coates Professor of Neurology and professor of neurobiology, is one of six scientists to receive the Senator Jacob Javits Award in the Neurosciences from the National Institute of Neurological Disorders and Stroke. Strittmatter's award will allow him to further study signaling pathways and loss of function studies in animal models of disease.

Edward M. Uchio, M.D., assistant professor of surgery (urology), received the 2005 Dennis W. Jahnigen Career Development Scholars Award. The two-year career development awards allow junior faculty to begin a career in the geriatric aspects of their discipline.

Raymond Yesner, M.D., professor emeritus and senior research scientist in pathology, received the Gold Medal from the United States and Canadian Academy of Pathology in May, one of the most prestigious awards in the field of pathology.

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

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A call to professionalism

As 100 new medical students begin their education, a physician defines the principles of their calling.

At the beginning of the White Coat Ceremony in August, Dean Robert J. Alpern, M.D., assured the 100 members of the Class of 2009 that they were where they belong. "The admissions committee did not make any careless errors in admitting you to our medical school," he told the crowd in Harkness Auditorium. "If we do our jobs, and you do yours, years from now students will walk these halls wondering if they belong in the same institution as the Class of 2009."

Before they received their white coats, keynote speaker David L. Coleman, M.D., HS '80, professor and interim chair of medicine, noted that the ceremony started in this country in 1993 as an effort to "acknowledge the professional ideals that are the essence of being a physician.

"Professionalism," Coleman continued, "drives how we live, how we aspire and how we learn. ... I have come to believe that it is the inseparable weaving of scientific discipline with humanism that is at the core of professionalism. We cannot and will not be humane physicians without employing science. And we cannot and will not be medically competent physicians without employing humanism."

The principles of professionalism rest on the pillars of nonmalevolence, beneficence, patient autonomy, justice, inquisitiveness, competence and teaching, Coleman said. They require, among other things, that physicians do no harm, advocate on behalf of patients rather than themselves, strive to do good, respect decisions made by patients and seek equity and justice in the delivery of care. "It should deeply



David Coleman, Nancy Angoff, Herbert Chase and James Jamieson were among the faculty helping students with their white coats.



Forrester Lee, assistant dean for multicultural affairs, welcomed Caleb Korngold to Yale.



Hasani Baharanyi donned his white coat for the first time.

BELOW Back row, Fabienne Meier-Abt, Katherine Uyhagi, Ellen Vollmer, Martin Dominguez and Corey Frucht; front row, Maya Kotas, Rachel Rosenstein, Julie Xanthopoulos and Sara Crager.

bother everyone in this room that 48 million Americans are without some form of health insurance," he said.

In concluding, Coleman cautioned the students to prepare to make sacrifices. "Medicine will require a great deal from each of you, and very importantly, it will give back a great deal to each of you," he said. "If you can find your balance while fulfilling the ideals of professionalism, you will attain the immeasurable and enduring rewards that your new profession offers. I hope your white coat will always inspire your aspirations and your ideals, from this day forward." —John Curtis





John Forrest helped Rebecca Bruccoleri on with her white coat.



Dean Robert Alpern welcomed Michelle Collins to the medical school.



Titilope Oduyebo after group portraits outside the Sterling Hall of Medicine.

Reunion 2005

Alumni see the artistic side of surgeons, hear a talk on terrorism and, as ever, catch up and relive old times.

Photographs by Terry Dagradi and John Curtis



Surgeon-artists James Dowaliby, John Anlyan, Ralph Greco, Bernard Siegel, Paul Barcewicz, Eiji Yanagisawa and Michael O'Brien displayed photographs, paintings and sculptures at the Surgical Society Spring Reunion in June. Although the reunion in June officially kicks off with a Friday evening dean's reception followed by the clambake on Harkness Lawn, in recent years a Thursday evening reunion of the Yale Surgical Society has increasingly drawn alumni to New Haven a day early. This year, early birds were treated to a discussion of the surgeon as artist. Other reunion talks included a discussion of terrorism by a psychiatrist who has worked with the Central Intelligence Agency (CIA) and a panel on advances in treatment of pediatric diseases. This year's reunion also saw the election of a new president and vice president of the Association of Yale Alumni in Medicine.

At the New Haven Lawn Club on Friday, public health alumni heard a panel on the impact of genomics on their profession and, over lunch, a keynote talk on the potential for genetics and biotechnology to improve the lives of the poor.

From surgeons to artists

As an adult Bernard S. Siegel, M.D., HS '61, returned to a boyhood hobby that had given him great pleasure. Painting, he said, is "a way of relieving the pressures of being a physician. It makes me lose track of time. I think it is the healthiest state I can be in." Siegel, whose paintings of his family and a self-portrait in surgical scrubs were on display in the Cushing/Whitney Medical Library in June, was one of three speakers on "The Surgeon as Artist," the theme of the 10th Annual Yale Surgical Society Spring Reunion in June.

Joining him in the discussion in Harkness Auditorium were surgeon

Dean Robert Alpern outlined the state of the school and plans for its future at the annual meeting of the alumni association.

and photographer James M. Dowaliby, M.D. '67, HS '72, associate clinical professor of surgery (otolaryngology), and surgeon and sculptor Ralph S. Greco, M.D. '68, HS '73, the Johnson & Johnson Distinguished Professor and chief of general surgery at the Stanford University School of Medicine.

Dowaliby has been taking pictures for 52 years. With his digital camera he documents family events and vacations and records his surgeries, but his personal and professional lives merged in this exhibit with two photographs of his sister-in-law as she prepared for radiotherapy to treat cancer. Dowaliby photographed her face as it was being fitted with a mask. He converted his color pictures to black and white, then increased the contrast to obtain stark, almost surreal images.

Unlike the other speakers, Grecoa professional sculptor for more than a decade, with gallery shows and sculptures in private collections around the country-said he has failed to find a link between surgery and his art. "I have searched in vain to find a connection that makes any sense to me between surgery and sculpture," he said. "Surgery is about the pursuit of technical perfection, sculpture about the pursuit of beauty. Perhaps what they have in common is that in both, as we learn, we come under the influence of masters who influence us in many ways, some of which are not easily recognized." Greco's representational and abstract stone sculptures were among the photographs, paintings and sculptures by nine surgeon-artists on display at the symposium.

Other works on display by Yale surgeon-artists included those of John



A. Anlyan, M.D. '45; Paul A. Barcewicz, M.D., assistant clinical professor of surgery (gastroenterology); Wayne O. Southwick, M.D., former chair of orthopaedics; Michael O'Brien, M.D., PH.D., assistant clinical professor of surgery (gastroenterology); Eiji Yanagisawa, M.D., HS '59, clinical professor of surgery (otolaryngology); and Ken Yanagisawa, M.D., HS '93, assistant clinical professor of surgery (otolaryngology).

Of tyrants and terrorists

Reunion activities started off Friday with a sobering presentation by psychiatrist and terrorism expert Jerrold M. Post, M.D. '60, who has profiled terrorists and tyrants for the CIA. Terrorists, he said, tend to be "normal individuals" who have more in common with urban gang members or mobsters than with crazed fanatics. Indeed, terrorist groups screen out emotionally unstable individuals because they represent a security risk.

"You can't explain terrorism on the level of individual psychology," said Post, director of the political psychology program at the George Washington University and founder of the CIA's Center for the Analysis of Personality and Political Behavior. The attractions of joining a terrorist group, he said, are rooted in collective psychologyalienated youth join to find purpose in their lives and they subordinate their individuality to the group cause as articulated by a destructive, charismatic leader such as Osama bin Laden. Group psychology binds the members together, and group and organizational psychology can push them to risky and destructive behavior, as they recognize that dissent leads to expulsion or death.



Jerrold Post discussed the psychology of terrorism, noting that terrorists are rarely crazed fanatics.



of the alumni association and Frank Lobo was elected president. Donald Moore (center) is past president.

MIDDLE Donald Moore, with his wife, Christine, and daughter, Crystal, ended his term as president of the Association of Yale Alumni in Medicine this year and was honored with the Distinguished Alumni Service Award.

BOTTOM Sherwin Nuland also received the Distinguished Alumni Service Award, for his outstanding dual careers as a surgeon and author.

Religious terrorists are spurred by an ideology of hate toward nonbelievers. Although their war on modern influences depends on modern technology, technology is not the key to fighting terrorism, said Post. He proposed a program of strategic communication designed to inhibit potential terrorists from joining the group, produce dissent in the group, facilitate exit from the group and reduce support for the group. But as he showed the photo of a 1-yearold child wearing the bomb-draped vest of a suicide bomber. he cautioned that the so-called war on terror will be decades long. "We have already lost a generation," he said. "Hatred and the attractions of martyrdom have been bred in the bone from childhood on."

The state of the school

After Post's talk, alumni moved up the street to the dean's reception in the Historical Library, followed by the clambake on Harkness Lawn.

The next morning the Association of Yale Alumni in Medicine (AYAM) elected Francis M. Lobo, M.D. '92, to a two-year term as president. Jocelyn S. Malkin, M.D. '52, HS '54, FW '60, was elected vice president. Christine A. Walsh, M.D. '73, elected two years ago to a three-year term as secretary, will continue in that position for another year.

Lobo said he is assuming the presidency at a moment of "tremendous excitement. ... The School of Medicine is seeing a vigorous expansion of the missions of research and patient care, as well as a very appropriate sensitivity to the special nature of our educational mission by Dean Robert Alpern. That will be a very exciting message to bring to the alumni," he said. Malkin, who is in private practice as a psychiatrist in Maryland, said, "I am particularly interested in the issue of women faculty, promoting equal working conditions and salaries for women." Malkin has served on the AYAM executive committee and as a delegate and member of the board of governors of the Association of Yale Alumni.

Outgoing AYAM president Donald E. Moore, M.D. '81, M.P.H. '81, and Sherwin B. Nuland, M.D. '55, Hs '61, each received the Distinguished Alumni Service Award at the Saturday morning business meeting. Moore was honored for his service to his community in Brooklyn, N.Y., where he has a private practice and makes house calls. "You have always put the patient first," read his citation, which also took note of his teaching of medicine and his leadership in "embracing the cultural diversity that is a vital part of our school's—and our nation's—growth."

Nuland was honored for his "distinguished and outstanding" career as a surgeon, and for his second career as a scholar, writer and lecturer in the history of medicine. His citation noted his humanitarianism as well. "When the Asian world was devastated by a tsunami, you immediately joined a Yale medical team to travel to Sri Lanka."

Following the awards, Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, discussed the state of the school, which he described as one of advancement and expansion. A strategic planning process begun last year has created new venues for communication and identified areas for allocation of resources. "The school cannot and should not invest in every conceivable area," Alpern said. "The areas in which it does invest should be truly excellent and among the best in the nation." Areas targeted for investment include faculty, new research and clinical programs, facilities, new research buildings, innovative medical education programs and student financial aid.

Childhood diseases grow up

Earlier that morning, at the annual scientific symposium, alumni heard from a panel of Yale researchers who are helping to rein in diseases that, in the not-too-distant past, presented parents with their worst possible nightmare: burying a young child.

Certain congenital heart defects, type 1 diabetes and cancer were often associated with poor outcomes, but "the tide is turning on those diseases," said Margaret K. Hostetter, M.D., the Jean McLean Wallace Professor of Pediatrics, chair of pediatrics, and moderator of the symposium *From Embryo to Young Adult: New Frontiers in Pediatrics.* Three Yale faculty members described their research.

Martina Brueckner, M.D., FW '90, is literally shining a light on the genetic roots of atrial isomerism—a condition in which the heart develops as a mirror image of its normal self. A team led by Brueckner, an associate professor of pediatrics (cardiology), discovered in mice that a "molecular motor" gene called left-right dynein, mapped in 1997, is crucial to a developing embryo's "biological handedness," the ability to tell left from right.

The process starts early. "By 56 days of human development, the heart is fully formed," Brueckner said. "Handedness" is determined as early as 20 days, and if it doesn't happen correctly it "can lead to a very, very malformed heart." By examining embryos under special lighting in a microscope, Brueckner's team discovered that the cells of the nodes (organizing centers) have hair-like structures called cilia that move fluid around the embryo leftwards, leading to asymmetric development of the heart. This doesn't happen in embryos with the mutated form of dynein.

While only one in 8,500 people is born with inverted organs—and many live a healthy life without ever knowing of the inversion—the condition strikes one in 25 of Brueckner's congenital heart patients. "They're what we call our frequent flyers," she said. "They keep coming back."

The progress against type 1 diabetes has come in several large waves the discovery of insulin in the 1920s and the advent of glucose self-monitoring in the 1970s—rather than incrementally. The next wave is the development of an artificial pancreas, which Stuart A. Weinzimer, M.D., an associate professor of pediatrics (endocrinology), called "our best shot" at diabetes management.

Researchers have two of the three elements needed, Weinzimer said. One is the insulin pump, developed at Yale in the 1970s, which is now portable enough (once the size and weight of a laptop computer, it is now no larger than a pager) to be in widespread use. A 2002 Yale study of the latest devices found that they cut episodes of hypoglycemia in half.

The second innovation is the round-the-clock glucose monitor. Some models can read blood sugar levels







TOP At the Saturday morning scientific symposium, Margaret Hostetter, chair of pediatrics, moderated a discussion of advances in the treatment of childhood diseases.

MIDDLE Martina Brueckner described her research into atrial isomerism, a condition in which the heart develops as a mirror image of its normal self.

BOTTOM Nina Kadan-Lottick directs a clinic that helps families deal with life after cancer. Many survivors of childhood cancer face health and psychological problems.

without puncturing the skin, and others sound an alarm when levels are abnormally high or low. While "we have a lot of work do to on these," Weinzimer said—they still don't give a completely accurate picture over a 24-hour period— "there is a place for them." The third component to creating an artificial pancreas, under study at Yale, uses a computer that gets the insulin pump and glucose monitor "to talk to one another," signaling the insulin pump to respond to a patient's individual needs. "We're getting closer and closer," he said.

In 1997, one in 640 Americans was a survivor of childhood cancer, and that rate is expected to rise to one in 250 in five years. The progress is such that doctors face a task their peers could only dream of a generation agocoping with problems faced by an ever-growing pool of childhood cancer survivors. "This is a growing population," said Nina S. Kadan-Lottick, м.р., an associate research scientist in pediatrics (hematology/oncology), but "there are costs." Many survivors have problems with growth and fertility, don't do well in school, have self-image problems, suffer from neurocognitive impairment, develop subsequent malignancies and live shorter lives. To help the survivors of childhood cancer, especially those recovering from leukemia, Kadan-Lottick directs the HEROS clinic, a unique clinical program within the section of pediatric hematology/ oncology at Yale.

Kadan-Lottick said her team is looking at the role of family strains, mechanisms of coping with life after cancer and what types of chemotherapy are more likely to lead to other medical problems later. "There are many opportunities for screening and intervention," she said. On the bright side, "cure is the rule, not the exception, for children with cancer."

Public health and the human genome

"Race is really a social phenomenon, not a biological one," said Kenneth K. Kidd, PH.D., professor of genetics, psychiatry and biology at Yale, the keynote speaker at alumni day at the School of Public Health, held at the Lawn Club on Friday, June 3. His speech kicked off a discussion of genomics and public health, an area in which health practitioners are still feeling their way.

Citing studies of 42 genetically diverse populations from around the world, from the Mbuti of Africa to the Yakut of Siberia, he said that despite obvious, skin-deep differences, the genetic diversity found within any given human population far outweighs the diversity between populations. Nearly all potential genetic variations are found in every population. "It's really impossible to define a boundary of a race based on these differences," he said.

Panelists at this year's public health reunion explored how the genomic revolution might be applied to epidemiology, while cautioning against overemphasizing genetic causes of disease and neglecting environmental and behavioral causes. At least two speakers said the promise of genomics has been "oversold" to the public. As Kidd stressed in his talk, there is still much to learn about human genetic variations.

The 400 or so variants he has studied represent a tiny, "Eurocentric" fraction of the estimated 6 million in the human genome. "We need to know how much variation there really is and how it is distributed around the world," he said, before genomic data can be used to relate human diversity to public health problems. As an example, he cited a study that appeared to link variants in the dopamine transporter to smoking in the United States population. But when he looked at the same gene in populations around the world, he found much more variation among the populations, irrespective of smoking, that called the original results into question.

Despite such caveats, public health professionals will be in the forefront of using genomic data, noted panel moderator Paul A. Locke, M.P.H. '80, J.D., DR.PH., a visiting scholar at Johns Hopkins. Five panelists described how genomics is already affecting their piece of the public health puzzle.

Alan Goldberg, PH.D., director of the Center for Alternatives to Animal Testing at Johns Hopkins, said genomics will eventually allow toxicologists to use fewer animals in tests. Genomics, he said, will lead to *in vitro* replacements "that are both good science and allow humaneness."

Lloyd M. Mueller, PH.D. '84, an epidemiologist at the Connecticut Department of Public Health, noted that genomics' impact on policy is "promising, but challenging to translate." And, he cautioned, this promise is oversold to the public. For example, said Mueller, the Connecticut Legislature recently mandated an expanded battery of newborn screening tests, some of which have not been systematically studied and yield test results that do not lead to specific treatment decisions. Audience members worried about the potential legal and ethical ramifications of tests with still-unknown false-positive and false-negative rates that are designed to detect diseases for which there are no known interventions.

Herbert Yu, M.D., PH.D., associate professor of epidemiology and director of Molecular Epidemiology Shared Resource at Yale Cancer Center, discussed the effects of heredity, lifestyle and environment on DNA methylation, a process involved in gene expression. Disruptions in methylation can cause disease, and Yu noted that methylation patterns can be inherited but can also be changed by environment, lifestyle and exposure to chemicals.

This interplay of behavior, environment and genetic luck was also addressed by Marta Gwinn, M.D., M.P.H., the director for science at the Office of Genomics and Disease Prevention at the Centers for Disease Control and Prevention, and Kathleen R. Merikangas, PH.D., senior investigator and chief of the Section on **Developmental Genetic Epidemiology** at the National Institute of Mental Health and a research affiliate in epidemiology at the School of Public Health, where she was a professor until 2003. The underlying heterogeneity in populations will allow doctors to distinguish between hereditary and sporadic cases of cancers or other diseases, and to identify subgroups that are more susceptible to environmental risk factors. "Risk factors coupled with genetics and biology become meaningful," said Merikangas.

She went on to add, however, that "genomics has been grossly oversold." Discoveries such as the putative "gene for smoking," she said, could make people feel they are absolved from



Keynote speaker Kenneth Kidd said genetic differences do not define race, which is a social rather than a biological construct.





Panelists discussing the implications of genomics for public health included, clockwise from top left, Kathleen Merikangas, Alan Goldberg, Lloyd Mueller and Herbert Yu.



In his luncheon address Peter Singer argued that genetics and biotechnology can improve the lives of the poor.

responsibility for their high-risk behaviors. "We need to help people understand and not overinterpret the role of genes," she said.

Past progress, future challenges

At the public health alumni day luncheon, Interim Dean Brian P. Leaderer, м.р.н. '71, рн.д. '75, began by praising his predecessor, Michael H. Merson, м.D., the Anna M.R. Lauder Professor of Public Health, who stepped down in December after 10 years as the first dean of public health at Yale. "I think it is really important to all of us as graduates to acknowledge what he has done," Leaderer said, citing a twofold increase in the size of the faculty, improved facilities, increased visibility for the school and the creation of the Center for Interdisciplinary Research on AIDS.

As the search continues for a new dean, however, a report from the provost's office has noted some areas for improvement. The report called for continuing a strong focus on research, an improved educational program and an examination of administrative structure, Leaderer said. And, the report said, the school lacks a critical mass. "We are too small and we lack the money and infrastructure to grow," Leaderer said. The subtext to this discussion, he added, was independence. EPH, which is accredited as a school of public health, has long sought to be free-standing, rather than a department of the medical school. "The university's response was that there will be no independence in the foreseeable future."

In response to the provost's report, the school has begun a strategic planning process. "We are paying more attention to the quality of our teaching," Leaderer said. The school is also planning a one-year master's program for those with a degree in healthrelated science. And a new program with Yale College would create a joint five-year program in which undergraduates could major in public health and after graduation spend another year obtaining an M.P.H.

Jerald A. Fagliano, PH.D., M.P.H. '85, was inducted into the Alumni Public Service Honor Roll for his service to Vermont and New Jersey in the area of environmental health. David A. Newman, м.р.н. '96, received the Eric W. Mood Alumni Award, established in 2005 to recognize an alumnus or alumna demonstrating outstanding promise as a new professional in public health. As corporate director of environment, health and safety at Millipore, a bioscience company headquartered in Billerica, Mass., he developed, implemented and evaluated programs for the company. James S. Marks, м.D., м.Р.н. '80, the senior vice president and director of the health group at the Robert Wood Johnson Foundation, received the Distinguished Alumni Service Award. He was previously in a top leadership post at the Centers for Disease Control and Prevention.

Marks said people often miss the connection between public health and their daily lives. "We have to make that connection—that screenings, getting your flu shot are connected to living the kind of life you want," he said.

"... those other 5 billion people ..."

After lunch, Peter A. Singer, м.D., м.р.н. '90, the Sun Life Financial Chair in Bioethics and director of the Joint



Centre for Bioethics at the University of Toronto, received the 2005 Award for Excellence. He began his remarks by pointing out the difference in life expectancy in the United States and sub-Saharan Africa. "Eighty years and rising and 40 years and falling. If that isn't the mother of all ethical challenges, what is?" he asked, before pondering how technology and genomics can improve global health. Showing a slide of children in a coastal village in India, he said, "They are all barefoot and they live in thatched houses. ... Right in the middle of their village is an information kiosk where they can access the Internet." The point, he continued, is "the potential of science and technology and innovation to better the lives of the poor. I want to argue that genetics and biotechnology have comparable, if not greater, potential."

As an example he pointed to "the largest mass poisoning in world history" in Bangladesh, where 50 million people are affected by exposure to arsenic in drinking water. At the bottom of the country's wells are bacteria responsible for the arsenic, he said. But in Australia there are bacteria that remove arsenic from water. Genomics, Singer said, has the potential to solve the problem in Bangladesh. Sequencing the genomes of these two bacteria could yield a way to offer a solution to the problem, he said.

"We need to keep the focus on those other 5 billion people in the world, those that have half the life expectancy of people in this room," Singer concluded.

60th reunion

Although time and tide and the vagaries of advancing years have diminished the numbers and vigor of this class, we had a splendid turnout, attracting more attendees than some classes junior to us.

Making the trip to New Haven were John and Betty Anlyan (basking in the glory of the greatest gift ever to the School of Medicine), Dick and Verne Breck (appropriately enjoying the reunion they orchestrated), Sandy Cockerell (with son Dr. Charles and lovely history professor daughter-inlaw Karen), Dick Dyer (whitehaired but otherwise unchanged since his glory days), Sid Feuerstein (looking tanned and terrific), Ray and Pat Gagliardi (still the prettiest girl who found her husband in the air raid shelter in the library), Bill and Marj Jenney (he is the dignified and impressive doctor type), Lee and Barbara Jones (no one had a more gorgeous caregiver than Barb), Mike and Geri Lau (upbeat and optimistic and just plain fun), Charlie and Laura McLean (with daughter Patti, who has inherited the best from both-Charlie introduced me to my lifelong addiction to golf). Our best surprise was Gove Hambidge, who was attending his first-ever reunion and had a great time. Gove still practices psychiatry full time in Golden Valley, Minn.

We shared the spectacular clambake dinner and sherry lunch; we toured the magnificent Anlyan Center and felt vicariously the pleasure that the donor was one of us; we took a tour of historic New Haven and heard some really informative lectures. Possibly the best was hearing from the new dean. He seems to be the right man in the right job at the right time. The city, the university and the medical school campus have made tremendous strides since last reunion. The future looks great.

Far and away the best of all, however, was the warm cama-

raderie of our group. It was almost as if it was June 1942, and we were young again. Our next reunion will be in 2010 and **Gove** has already committed to come. I hope the rest will do the same.

Ray Gagliardi

1955

50th reunion

There are by our last count 60 living members of our class. A total of 30 were able to attend the reunion for at least one day, and most for three days. Leo Cardillo, who is still in practice, was able to come for only a short time on Friday, but his presence brought our total attendance to 50 percent. Alan Stone was only able to come for Saturday, but also was a welcome face. (He still looks like he did 50 years ago.)

The committee had made a number of phone calls to members who had not responded to the initial letters. It was really nice to talk to them, but unfortunately the reasons for not coming were usually because of illness of the classmate or spouse. Some were quite ill, but as physicians, we would expect this in a group of people in their 70s. What was encouraging was the general overall health of our group. Almost everyone is retired and finding many interesting and productive pursuits to keep them busy.

The week after the reunion, I went to Atlanta for another event, and was able to have lunch with **Roger Lester**, who could not come to the reunion because of another commitment. He is doing some scholarly work in history and philosophy, and was giving some lectures the weekend of the reunion. He will be at the 55th.

Again, one of our classmates was honored; **Shep Nuland** received the Distinguished Alumni Service Award. As usual, he was gracious and articulate in his acceptance speech.

We were fortunate in having our oldest classmate, **Pat Costa**,

attending as well as our youngest, **Guy McKhann. Harry Kendall** and **Sandy Zuckerbraun** traveled from distant California with Wanda and Ruth to attend. **Sandy** is still in practice and because he sees many Mexican-Americans, he has become fluent in Spanish. You see, you can teach an old horse new tricks.

Frank Johnson is retired, but still lives in the vast outreaches of Montana. Milt Corn was in from Bethesda, Md., where he is active in what seems like an important but somewhat confusing project at the NIH. I'm sure with his involvement it is important.

Jim Garlington is now working on a project to collect digital pictures from the reunion and also some from people who could not attend. He is going to put them on a CD and send it to all class members. I thought it was a great idea, and he is to be congratulated for this work. See you at the 55th.

Jack Landau

1960

45th reunion

Our 45th reunion was a source of great pride for the Class of 1960, because the keynote speaker for the entire alumni body was our own Jerry Post. Jerry, a distinguished professor of psychiatry and political science at George Washington University, has written six wellreceived books on subjects ranging from the psychopathology of political leaders to the origin and perpetuation of terrorism. Many of us had already been familiar with his thinking not only from his books, but also from his numerous appearances on cable TV.

On Friday afternoon Jerry spoke eloquently and unsettlingly about the rapid propagation and intensification of terrorism. His talk, subtitled "When Hatred Is Bred Into the Bone," highlighted the bitter irony that our political leaders are confidently adopting bellicose policies that are only mak-









ing the phenomenon worse. The fact that there are no panaceas and that terrorism will be with us for generations to come was deeply troubling to the audience; this struck us as the mark of a highly successful talk.

The festivities continued into the evening. During the clambake, which seems to get more delicious each time, we began to unwind and renew our old friendships. There was general agreement that the finalists for the Obscenely Young Forever category were Gerald Cimmino, Neil Cooper and Sue Kleeman. By virtue of his continued stature as basketball star, Lanny Ames was charitably awarded honorable mention. Moreover, Cooper had lost so much weight that no one recognized him. We suspected they were all plants from the Class of 1990. However, the rest of us all looked so fit and terrific that no one really envied them, except for Kleeman. The Most Eloquent Award went to Bob Wallach, whose brave and moving reminiscences brought many of us to tears.

On Saturday we were all pleased by Dean Alpern's talk. It seemed engaged, thoughtful, serious and leaderly. We were persuaded that our school is in very good hands and will retain its outstanding rank for years to come.

But the *pièce de résistance* was, as always, the Saturday evening dinner at the Lawn Club. The tone was set by class agent **Tom Kugelman**, who reported that our class had contributed more than any other reunion class to the Annual Fund. This was due in large measure to one extremely large gift from **Eric Kindwall**, who spoke movingly of what Yale had meant to him.

And so did the rest of us. We all got up in turn and gave accounts of ourselves and our lives. One common thread was that in many different ways, even for those of us who felt we had not thrived within the Yale System and had not been happy here, the Yale experience had

somehow defined us-or more accurately, had helped us define ourselves-and helped us become what we are today. We discovered that on our first day of school each of us had been convinced that Yale had made a mistake in admitting us, and that each of us was convinced that he or she was the only one who felt that way. And over time we discovered that each of us had been wrong. That's quite a tribute to Art Ebbert and the late Tom Forbes—not to mention all the rest of our splendid faculty.

Jerry led us in observing a brief silence in honor of our deceased classmates: Ormond Brody, Tom Carson, Stan Chung, Dave Dunn, Mal Golden, Irv Guttenberg, Arthur Martin, Kent Morest, Mike Moynihan, Ross Snyder, John St. Andre and Brian Welch.

Present at this extraordinary occasion were Vic and Laura Altshul, Lanny Ames, Neil and Teresa Cooper, Jon and Carol Courtney, Jim and Kitty Eustermann, Gene Gaenslen, Jim Gilman, Bill Kaden, Eric Kindwall, Sue Kleeman, Tom and Alice Kugelman, Tom Lau, Bob Marcus and friend Vie Simons, Al and Barbara Newcomb, Tom and Danielle Okin, Fred and Ruth Palace, Jerry and Carolyn Post, Nancy and Bill Powell, Buzz Robinson, Al Ross and friend Jane Semmons, Dan and Lina Rubin, John and Suzanne Schrogie, Bob and Judy Wallach, May and George Wang, and Ron Yankee. Present in spirit was Malin Dollinger, who had intended to come before his wife. Lenore's. sudden illness and who sent a warm and moving account of his recent life.

Victor A. Altshul

1965

40th reunion

The Class of '65 had a wonderful 40th reunion in early June. We enjoyed the traditional shore dinner under the tent at Harkness, and a lovely dinner at the Quinnipiack Club on Saturday. Twenty classmates made it back and enjoyed catching up—some have been regulars at reunions, others first-timers. Attendees included Amy and Tom Aoki, John Coyle, Greg Culley, Mike and Susan Cummings, Carl and Emi Ellenberger, Chris Gates, Frank and Donna Grady, Gary Gross and Betsy Shure, Bob and Donna Gryboski, Reed and Ellie Heffner, Dave Hill, Edgar and Ellen Hull, Carl Hunt and Joyce Shoemaker, Ron Karpick, Mohandas and Joanne Kini, Larry and Linda Ossias, Bob and Mary Pickens, and John and Greta Seashore. Five of us have retired and some have switched career paths, but most are still practicing medicine actively. Just can't keep this group down. There was considerable sentiment for having the occasional mini-reunion more frequently, especially for those of us who live relatively near each other. Perhaps we Northeasterners could gather at Carl Ellenbergers' Mt. Gretna (Pa.) music festival next summer. If anyone is interested, let me know (john.seashore@yale.edu). Is anyone on the West Coast up for organizing something out that way? We hope to see even more people next time around. John Seashore

1970

35th reunion

Our class reunion dinner was held in the library of the Quinnipiack Club on Saturday evening and attended by 15 members as well as their spouses and guests. Following numerous photo shoots to accommodate late-arriving members, we enjoyed an excellent dinner and had a nice time catching up on the personal and professional lives of what was truly an eclectic class. The attendees included Elissa and Dan Arons, John Blanton and Beth Balschi, Paul and Judy Braun, Romney and Mary Sue Burke, Anne Curtis, Jonathan and Rosanne Ecker, Rick and Ruth Edelson, Harvey Fernbach and Ann Birk, Tom Gouge, Paul and Patricia Hessler, Gerry Kennealey, Mark and Susan Korsten, Bob and Joan Rosa, Joellen Werne, and Karl and Diane Wustrack, as well as special guest Rose Papac. Rose, one of the outstanding educators and clinicians from the classical era of Yale medical school, announced that she will be retiring this July and plans to concentrate her efforts on writing, including a book. All of her many grateful students wish her well. I will be sending out a composite of e-mails I have received that provides specific information about many members of our class. If you do not receive this communication and wish to obtain it, please contact me (rrosa@northwestern.edu).

Bob Rosa

1975 30th reunion

Once again, it was quality, not quantity in attendance, that had us all having a good time at new New Haven restaurant L'Orcio for our Saturday dinner. Liz Gawron and Paul Johnson came all the way from California. Paul is an expert diver and scuba instructor as well as an underwater photographer. Brendan **Clifford**, too, came in from the California beaches, noting he has retired from his surgical career-he will be spending some time this fall with his wife in Massachusetts. Dawn Hassinger came up from Atlanta. Dawn spends her time doing medical writing these days. Vivian Reznik spent several days visiting with me. Besides doing academic pediatrics at the University of California-San Diego, she is researching a book on the beginnings of coeducation at Yale. Vivian and I were especially upset that Barbara Stoll, who has just been named chair of peds at Emory, didn't make it up for the event-we were hoping we could cause just as much trouble as we used to. The more local contingent was Mark and Sharon Ruchman, coming down from Washington, Conn. Mark is a very active ophthalmologist in Waterbury. And Frank Watkins, who is an

orthopaedic surgeon, came up from New Rochelle, and even though his lovely wife is a lawyer, we all had a good time. I have just recently given up obstetrics, only because of the malpractice insurance—and I spend the time I should be delivering babies harassing as many politicians as I possibly can.

We did receive some "regrets" with information. Hymie Milstein is still happily practicing internal medicine at Kaiser in LA—one suggestion is that we should hold a reunion out there, with so many classmates there. Kathy Shepard is taking time off from pediatrics to spend the year in Italy with her husband, the newly retired dean of the Law School at Duquesne University. And George Noble was busy at many family graduations around central lowa, where he is busy doing peds surgery. Sid Spiesel's peds practice in New Haven is still very busy, but he couldn't come to the reunion because his family held a 65th birthday party for him that evening.

However, what I found most gratifying at the reunion was seeing our professors—folks like Dr. Braverman and Dr. Kushlan having a good time, still practicing and teaching and reassuring me that we all have a lot of time left to have fun. And **Vivian** and I have a mission for the next reunion—to raise a bundle of money for the reunion fund more on that in subsequent mailings!

Mary Jane Minkin

1980

25th reunion

Our 25th reunion was graced by good weather and a good crowd. Twenty-one classmates came, many with their spouses, and some with children. We enjoyed the traditional clambake Friday night, the sherry lunch Saturday and a wonderful class dinner at the Quinnipiack Club. The dinner was made special as each classmate shared memories and updated the group on the events of their life over the last 25 years—it barely seems possible as most people looked very much the same.

The California contingent included Sittiporn Bencharit and wife Reylina. They have two children. Sittiporn has been happily engaged in a private GI practice for 18 years. He says, "Keep in touch, be here at the 50th and support the medical school." Cesar Molina, irrepressible as ever, came with wife Linda from Los Altos. He has a satisfying career as a cardiologist and still meditates. He was eager to show photos of his two daughters. Of special note, Cesar has a winery for sale and he provided samples of his award-winning wine at the class dinner. Nancy Todes Taylor is assistant chief of dermatology with the Permanente Medical Group in San Rafael, Calif., where she does mostly laser, skin cancer and cosmetic dermatology. She and husband Graham have two children. She goes to Australia (where her husband comes from) "almost all the time."

The mid-section of the country was represented by Walter Williams, who is a professor of radiology at University of Arizona Medical School. Walter had the honor of seeing one of his two sons, Steven Williams, M.D. '98, finish this year as chief resident in plastic surgery at Yale. Walter also reports that he has a serious hobby as an amateur radio operator. Craig Brooks passed through at the class dinner and recounted some of his adventures working as an ER physician for Aramco in Saudi Arabia for the last 12 years. Craig, his wife, Agneta, and their two children are moving to Colorado (someone has to keep those ski slopes busy!).

From Miami came **Eddie Alfonso**, one of our stalwart class agents, and wife Molly along with one of their children, Eduardo. **Eddie** is busy as a professor at the Bascom Palmer Eye Institute. **Eddie** and Molly have two other children, well into their 20s and engaged now in challenging careers. **Patricia Brown**, from Bethesda, Md., has experienced a number of transitions this year. "With the death of my father, I'm now a middle-aged orphan." Another change has been taking on a new position at the FDA reviewing new medicines for dermatology, while at the same time maintaining a toehold in clinical practice.

The Big Apple contingent included Al Siu, who is professor and chair of geriatrics at the Mount Sinai School of Medicine. AI and wife Margaret have two fairly young children. AI proved his devotion to them by wishing them goodnight by cell phone at the Friday clambake. Jonathan Jacobs dropped by for the class dinner. He is professor of general internal medicine at Cornell. He and his wife, Carolyn, have two boys. Jonathan is proud to have been able to start a \$75 million AIDS treatment program in New York City as well as a program in Nigeria. David Goldberg is busy in nearby New Jersey with his skin laser and surgery practice. He and wife Rachel have four children, one of whom wants to be a doctor despite today's challenges to the profession.

Never having left the comforts of New Haven are Gary and Debbie Dyett Desir. Gary, a nephrologist, is chief of medicine at the Connecticut VA Healthcare System, West Haven campus, and associate chief at Yale. Debbie is a rheumatologist in private practice. Together they have four children. Gary recalled how he met his wife while sharing an anatomy table. Jean Bolognia is professor of dermatology at Yale and her husband, Dennis Cooper, is also on the faculty, in oncology. Inside sources tell us Jean has become well-known within the specialty of dermatology for serving in a number of leadership positions and for having been the co-editor of what is becoming a popular dermatology textbook. Ann (Henderson) Hoeffer, social chair for this reunion and greatly appreciated, continues to be happy in her private pediatric practice. Ann and husband Ben

















Bradburn have two daughters. Larry Young and wife Lynn Tanoue (M.D. '82) have three children. Larry is a professor of medicine in cardiology and Lynn is a pulmonologist. Larry states that it is special to be a part of the university community. Barbara Fallon and husband Bennett Bernblum live in nearby Old Lyme, Conn., and have two children. Barbara is in private practice in oncology and an assistant professor at the University of Connecticut. Rose Papac was Barbara's mentor at Yale.

Marty Silverstein, from Newton, Mass., has a continuing career with the Boston Consulting Group. He helps biotech and biopharm companies improve their product development process. He and wife Andree, a dermatologist, have two children. Mary Hill Wise from Rochester, N.Y., came to the reunion on Friday. She practices holistic medicine and with husband Robert has four children.

The final crew consists of three classmates who graduated in 1981 but maintain ties to the Class of 1980. Phil Lee and his wife, Diane, share a psychiatry practice in New York City and together have two children. Charles Shana is a gastroenterologist in practice for the past 15 years in Newport, R.I., and Fall River, Mass. He and wife Miriam have two sons. Donald Moore, wife Christine and daughters were present at many reunion events. Donald practices internal medicine and is on the faculty at Cornell. Donald also is past president of the Association of Yale Alumni in Medicine and was honored to receive the Distinguished Alumni Service Award.

OK, you laggards out there: you missed a good time (and some really fine wine). The 30th is only five years away, so mark your calendars now. See you all there.

Patricia Brown

1985 20th reunion

Returning members of the Class of 1985 gathered for dinner at

the home of pediatrician JoAnne Burger. While the reunion dinner was scheduled for Saturday, Brian Lombardo (ever the eager beaver) got a jump on his classmates by showing up on Friday night. Brian is doing general practice in southern Vermont, having recently returned with his family from an extraordinary sabbatical experience during which he worked at a hospital in Kigali, Rwanda. Saturday's festivities reunited another dozen or so classmates, including ophthalmologist Kimball Woodward, who is practicing in Middletown, N.Y., and pediatrician Fred Santoro, whose practice is based in East Lyme, Conn. The passage of time has not altered Fred's trademark laugh. Pediatric endocrinologist Jon Nakamoto has joined Quest Diagnostics. He and his family came in from the West Coast for a week of med school and college reunions. Jonathan Lewin has moved from Cleveland to Baltimore to assume the chairmanship of the Johns Hopkins department of diagnostic imaging, a position only recently vacated by the current director of the NIH. Gail Mattson-Gates is a plastic and reconstructive surgeon in Los Angeles, and she strenuously denies participating in any Hollywood extreme makeovers. Sam Goos is also plying the skin trade as a dermatologist, with a growing multisite practice in the Boston area. The Boston contingent included Guy Fish, who is working in venture capital, and Sue Korrick, who is on the faculty at Harvard and focusing her efforts on occupational medicine and exposure to environmental toxins. Prolific author Bob Klitzman is on the psychiatry and bioethics faculty at Columbia. He has written several books and has participated in television documentaries. Jackie Gutmann, who is a fertility specialist in Philadelphia, blew out of a bar mitzvah before the waiters brought in the flaming desserts and raced to Connecticut in time to join the gathering. JoAnne was very gratified to

have her entire anatomy foursome reunited (although the group's cadaver was otherwise engaged). The group included ENT Barb Guillette, who came down from Providence. and rheumatologist Paula Rackoff, who came up from Manhattan. Completing the anatomy quartet was Jeff Lowell, who has acquired a fascinating skill set. In addition to serving on the faculty of Washington University in St. Louis as a liver and kidney transplant surgeon, Jeff has been trained by the St. Louis police as a hostage negotiator and spent time working on disaster planning for the Department of Homeland Security. Harrison Ford has expressed interest in portraying Jeff when filming begins on the movie version of his life. The evening ended with the general agreement that the entire class still looks fabulous, is a lot of fun to be around and should get together more often.

JoAnne Burger

1990

15th reunion

Some people may feel that the 15th reunion wasn't worth attending, but those of us who made it had a good time. It was my first time seeing my classmates and my first time back to New Haven since graduation, and much has changed. I couldn't believe that Grand Central had changed to a Walgreen's and Barnes and Noble bought out the Yale Co-op.

I also had a chance to tour the new Anlyan Center—home to the new anatomy lab and one of the largest buildings on the Yale campus. It is second only to the Payne Whitney gym in size and holds educational space as well as research labs.

Fortunately, none of our classmates have changed much! I caught up with **Nancy Angoff** and her husband, Ron, early on. As you all know, she is now the associate dean for student affairs for the medical school but for us, she's still known as "mom." **Will Andrews** made it from Boston with his family. **Will** still spends time with his private practice, but I believe he spends more time as senior medical director of Sepracor.

Chandler Samy came up from Ocala, Fla., with his family. He is a retinal surgeon in private practice. **Jonathan Foster**, an ob/gyn in Waterbury, came in with his wife and parents. His father was present for his 50th reunion.

New York was wellrepresented at our class dinner on Saturday. Sam Colin came in with his wife. He spends much of his time managing a health care investment fund with First Manhattan Co. Ethan Halm also made it. He is the chair of medicine at Mount Sinai. Finally, Julia Schillinger also drove up from New York. She is director of surveillance, epidemiology and research at the New York City Department of Health and Mental Hygiene, Bureau of Sexually Transmitted Disease Control. Her business card is the size of a postcard!

Robin Hornung probably wins the award for the longest trek to be with us. She came from Seattle by herself—but brought plenty of pictures of her son and husband. She is the head of pediatric dermatology at the University of Washington. Ercem Atillasoy (he'll always be known as **Tilly** to us) came from Philadelphia. Tilly is a dermatologist and the director of internal medicine, dermatology and tissue engineering at Novartis Pharmaceuticals Corp. We also had a chance to catch up with Jennifer Mark, who came in for the dinner. She's been busy in an ER in New England (I can't remember just where—a good reason for me to make it to the 20th).

Finally, I came in by myself from Concord, N. C. There, I am an electrophysiologist with a group of eight other cardiologists at a moderate sized community hospital. I am married to Jane Rasmussen (Class of '89) and have twin 9-year-old daughters! Overall, all had fun, but the evening did have a bit of a sad note. **Dan Stryer** passed away from a brain tumor this spring. He really had wanted to make the reunion, which filled us all with a certain sadness. We all decided that we wanted to do something meaningful in his name. I believe **Nancy** and **Tilly** are going to come up with some ideas. We need to move on this to make it really meaningful. Stay tuned for more information about this later.

Well, that's it. I hope to see more of you at the 20th reunion! Tom Christopher

1995

10th reunion

I am glad to report a strong turnout for the Class of 1995. It was wonderful, considering how busy we all are with our careers and families. Chris Lykins traveled from his busy otolaryngology practice in Phoenix to share memories with his friends. Chris has found a great spot for all of us to visit in Arizona and invites us all to visit him at Burning Man next year. Chris Wahl traveled from the University of Washington in Seattle. It was really an expedition, since his five-month-old triplets accompanied him. His wife, Rebecca, deserves most of that praise. Although we are sad that Chris has left the Yale community, we are happy to see that he is practicing sports medicine at the very institution that he once passed on. Emily (Rosenberg) Roth (pediatrics) and Jake Roth (psychiatry) were able to join us at the clambake. They and their two children spent the past few years at Harvard. No degrees for the children thus far. They have all recently headed for warmer weather near Todd Alamin and Artis Montague in California. David Morales, his wife, Mary, and their two children traveled from Houston, where Dave is a pediatric cardiothoracic surgeon, after nine years of training. Nick Schwartz and his wife, Loretta, traveled from Seattle for the

occasion. Nick is truly remarkable for being our only alumnus to have completed two residencies. However, most of us do believe that he is best suited for psychiatry. While he did not stay at the President's mansion we understand that his quarters in New Haven were comfortable. Jeff Algazy and his lovely wife, Abbey, came up from New Jersey for the event. Jeff has been doing consulting for a number of years and is happy spending time with his daughter. Brian Adams, Jilda Vargus and their daughter came back to Yale from Cincinnati. Brian is practicing dermatology and Jilda is practicing psychiatry. Brian and Jilda both exemplify the spirit of our class. Their assistance with fund-raising was appreciated by all of us. Tim Kinkead and his wife, Lisa, drove in from Cape Cod, where **Tim** is practicing orthopaedics. Tim now has a look-alike son, who fortunately has his mother's temperament. Christine Brozowski came 3,000 miles, from Berkeley. Her knowledge of wine makes her a very useful contact when traveling to Napa. My neighbor Jon Driscoll came with his wife, Jenna, and their 4-month-old twins. Jon has a great orthopaedic practice in Connecticut. He is even operating on fellow alumni! It was great to see Margi Rosenthal in attendance. Although difficult events brought her back to New Haven, we are glad to see her practicing pediatrics at Yale. Chip Skowron and his wife, Cheryl, came in from Greenwich to catch up with old friends. Chip is happily running a successful hedge fund, and has three children. As for myself, I am living on a farm with my wife, Holly, and our two children. I also practice pediatrics on the side.

It was really wonderful seeing everyone back at Yale. It was inspiring to see how far people traveled—particularly with kids! I am looking forward to seeing more of us back in the coming years. **Barbara Garcia**, **Alice Chang**, **Ben LeBlanc**, **Erin LeBlanc**, **Eric Hughes**, Larry Solomon, Tim Hong,

















Steven Craig

2000

5th reunion

The Class of 2000 turned out in good numbers for our first reunion, with slightly under 20 percent of the class in attendance. While most attendees were from the Northeast, we had a few long-distance travelers as well. Not too bad considering many are still in training. The weekend offered fine weather for the traditional New England clambake on Harkness Lawn, and a spectacular dinner hosted by the 50th reunion class at the Graduate Club. Our class has embarked on a wide range of paths since leaving Yale five years ago.

Jen Dorosz was on an East Coast swing, having finished her first year of cardiology fellowship at the University of Michigan. She spent an extra year in Seattle as chief resident at the University of Washington. Arvind Venkat is now an emergency medicine attending at the University of Pittsburgh. He was accompanied by his wife, Veena, who is finishing a pediatric GI fellowship, and their 6-monthold daughter. Jonathan Erulkar was recently married to Dierdre Carrol (YSN '00) and is now completing his orthopaedic training. Next year he will join the Boston crowd as he pursues a spine fellowship at New England Baptist.

The New Haven residents were well-represented. **Oscar Colegio** has finished a preliminary year in internal medicine at YNHH and will go on to train in dermatology at Yale next year. He is married to Stephanie Colegio-Eisenbarth, who will be going on to a residency in laboratory medicine. **Dan Negoianu** has completed his chief residency year at YNHH and will leave the Elm City for a nephrology fellowship at the University of Pennsylvania. **Michelle Mak** and her husband came to the clambake with their beautiful baby; **Michelle** is practicing dermatology in Bridgeport. **Andrew White** is finishing his orthopaedic training, with plans to start a spine fellowship in July. **John Mahoney** braved the weekend with his wife and their infant son Jack, all before driving across the country to start a hand surgery fellowship in California.

Joanna Sheinfeld and her husband, Mark Paltrowitz, are the proud parents of Leila. Joanna just finished her geriatrics fellowship at Yale and will be returning to Mt. Sinai, where she was chief resident along with Dan Jacoby. Dan and his wife, Stephanie, live in New York, where Dan is pursuing fellowship training in cardiology at Columbia. Joanna will be practicing alongside Jon Ripp as part of Mt. Sinai's Visiting Doctors Program, which cares for homebound elderly in New York City. Jon and his wife, Melissa, spent a year practicing in Alaska before returning to New York.

Other New York attendees included **Keri Adelson** and David Grodberg; **Keri** is juggling a fellowship in hematology and oncology at Columbia with taking care of Paley, an adorable toddler. **Maya Salameh**, having also finished a chief residency year at YNHH, will be moving to New York to practice vascular medicine at Columbia. **Jodi** and **Elie Levine** have three daughters; **Jodi** is completing training in dermatology and **Elie** is finishing his residency in plastic surgery.

Members of the Boston contingent were distressed that they had to come to New Haven to meet up. **Amy Nuernberg**, another YNHH chief resident, is completing a fellowship in occupational health at the Harvard School of Public Health, and will go on to a fellowship in pulmonary and critical care. **John Abraham** is finishing up his residency in orthopaedic surgery, and will go on to specialize in orthopaedic oncology. Karin Andersson is finishing up her clinical year in a GI fellowship at Massachusetts General Hospital (MGH); she is married to Brett Cohen, who was also in New Haven for his 10th college reunion. Deborah Wexler is finishing up her chief residency year at MGH before continuing her fellowship in endocrinology. Her husband, David Friedman, is very happy to be back in the lab after finishing his training in nephrology. Carl Seashore is practicing primary care pediatrics and working in the pediatric hospitalist program at MassGeneral Hospital for Children. His son, Luke, enjoyed the time with his grandparents as well as all the festivities.

There were day trips, mountain bike rides, scenic tours and even lectures spread over the weekend for all to enjoy. It was truly wonderful to catch up with so many old friends, and see how we, as well as New Haven, have all changed in five short years. We hope to see more of you at the 10th.

Deborah Wexler Carl Seashore

PA Program

In June alumni of Yale's Physician Associate (PA) Program held their first reunion, bringing together graduates from the program's 35 years. The reunion is expected to become an annual event, said Mary L. Warner, PA-C, M.M.SC., program director and assistant dean. "Every year we will have a dinner and invite our graduates to participate in activities throughout the medical school."

About 50 graduates renewed friendships and made new ones at the Graduate Club. Warner also described the state of the program: its accreditation was renewed last year, and thanks to a change in school policy, PA faculty now have the standing of clinician-educator track faculty. And, Warner said, an alumni outreach program is in the planning and development stages.

From Yale to Africa, an alumna finds her niche

A decade after her graduation, Rachel Bronzan studies malaria in Malawi.

On a typical morning in Malawi's rainy season, which runs from November to May and brings mosquitoes out in force, **Rachel N. Bronzan**, M.D. '95, M.P.H., sees patients with severe malaria. "It's sort of a perverse lottery jackpot," said Bronzan of the ward she works on at Queen Elizabeth Central Hospital in the city of Blantyre. "We can provide better care because we have fewer patients, but you have to be very, very sick to come to our ward."

In the dry season, Bronzan puts on her public health hat—she works for the Centers for Disease Control and Prevention (CDC) on epidemiological studies and disease monitoring for Malawi's National Malaria Control Program.

It is in Malawi that Bronzan has combined her love of Africa with an interest in science and a desire to use medicine to help others. Malawi, in southeastern Africa, has been her home since 2002, but Bronzan's interest in Africa started long before. "When I was young I was always taken with the idea of Africa—its natural beauty, diverse indigenous cultures, exotic wildlife and vast expanses of land and sky," she said.

She first traveled to Africa in 1991 as a Downs fellow studying HIV in Senegal. During her fourth year at Yale she went to Kenya for a clinical rotation and worked at a malaria research post. Now Bronzan lives in Blantyre, the commercial and industrial center of Malawi, a landlocked country of 94,000 square kilometers of rolling plains with meandering rivers, vibrant green tea plantations and peaked highlands bounded by Mozambique, Zambia and Tanzania.

Bronzan's foray into medicine seems natural when you understand her beginnings. Her father, a theoretical particle physicist, taught at Rutgers, and her mother, a clinical social worker, counseled psychiatric inpatients. She absorbed her father's methodical, logical approach to problem solving and her mother's nurturance and respect for others. Growing up with a younger brother only a half-mile from their maternal grandparents, she was also inspired by her grandfather, a physicist who worked on the development of color television at RCA. In his basement workshop they blew glass, built and detonated small cannons using compressed gas to fire bits of pencils and erasers, and created electromagnetic fields with wire coils (like an MRI) in which Bronzan's grandfather tested the effect on his vision.

In 1990, after graduating from Stanford with a degree in chemistry and working in an infectious disease lab, Bronzan began medical school. By her fourth year she still felt the lure of research, but during her travels in Kenya she saw the rewards of treating patients. "I was impressed by the great impact that the family physicians made, with broad training and simple interventions skillfully applied in a resource-poor setting. I realized that if I were to practice medicine I would most likely do it in a setting like that, where basic need is high," she said. She spent a fifth year at Yale, during which she got an м.р.н. at Harvard, and in 1995 began a residency in California at the Community Hospital of Santa Rosa.

After working at hospitals in the Bay Area, Bronzan applied to the CDC's Epidemic Intelligence Service (EIS), which provides on-the-job training in epidemiology. While waiting for her first posting, she traveled to Malawi to care for seriously ill children at Queen Elizabeth Central Hospital with Terrie Taylor, D.O., a professor of internal medicine at Michigan State University. For six months she received housing and a \$100 weekly stipend. "I thought this was a fantastic offer, although some of my friends wondered why I would be so happy about such a dramatic salary cut," she said.

In July 2000 Bronzan started her job at EIS, which over the next two



Rachel Bronzan took time out from her clinical and laboratory duties for a trip to Mt. Mulanje, the largest and highest mountain in Malawi.

years took her to Mali, Kazakhstan, South Africa and Florida for work in infectious diseases.

Now, along with her malaria research, Bronzan works as a part-time clinician-researcher for Taylor. "What is unique about my position is that it allows me the opportunity to do clinical care of severely ill children, clinically related research, as well as field surveys and public health-related projects," said Bronzan.

Her epidemiological studies and program planning could affect malaria control in Africa and abroad, but she finds that caring for children afflicted with malaria is her true reward. "Although mortality is high—between 15 and 20 percent of comatose children die—those who survive tend to recover quite quickly, and the majority of them do not have long-term neurological or developmental problems. They come to the hospital in a severe coma and can walk home in as little as two or three days. That in itself is really exciting."

—Kara Nyberg

Alumni FACES

A pediatrician who treated not just the children, but the whole family

As a research fellow at Yale in 1948, **Morris A. Wessel**, M.D. '43, joined in the landmark "rooming-in" study by the late clinical professor Edith B. Jackson, M.D., which examined how keeping newborns in their mothers' hospital rooms affected families. His participation in the study also helped Wessel decide what kind of pediatrician he wanted to be.

His role in the study was to interview parents during pregnancy. Mothers- and fathers-to-be often burst into tears as they recounted traumatic childhood incidents such as the death of a parent. "Is there any way that we as pediatricians could support families during a crisis like that?" he asked himself.

Jackson and Grover F. Powers, M.D., who headed Yale's pediatric department in Wessel's student days, also led him to a broader notion of his role as a pediatrician. "Anything that affects the child's welfare is within the realm of the pediatrician's responsibility," Powers said. After graduating from the School of Medicine, Wessel worked at the Mayo Clinic under Benjamin M. Spock, M.D., MED '29, whom Wessel considered a mentor throughout his career. Wessel's training was informed by his own childhood experience. The loss of his father when he was only 11 months old and his own "various sicknesses and unhappinesses as a child" convinced him that young people needed friends and advocates whose commitment did not stop at the office door.

He found a like-minded partner in another young pediatrician, Robert G. LaCamera, M.D., FW '56, and in 1951 started a practice marked by extraordinary involvement in the lives of families and by a commitment to improve the community.

"They were always late," laughed Donna Sandillo, R.N., their longtime practice manager. They were late because they made house calls and dashed across the street to the hospital—the office was on Howard Avenue—when one of their patients was in trouble.

"People waited for them," she said. "They understood."

The doctors encouraged parents to call when they faced any major challenge—medical or not. Families appreciated touches like handwritten notes on the anniversary of a death and calls to check on teens adjusting to college. New Haven is a city of rich and poor families, and the practice saw both. They accepted homemade pies as payment for an office visit.

Wessel spread his philosophy as a clinical professor at Yale and through his writings. In 1963, he published "Why Can't Mothers Stay in Hospital With Their Children?" in *Redbook*. Mothers across the country waved the magazine in hospital admitting offices demanding, "Where's my bed? Dr. Wessel says I should stay!"

"I was not very popular," he said, ducking his head to hide a grin.

Together with Anthony Dominski, PH.D., a scientist from the School of Forestry & Environmental Studies, he investigated lead levels in children in the 1970s and recommended a level then thought to be unrealistically low. Eventually the American Academy of Pediatrics recommended an even lower level.

With former Yale School of Nursing Dean Florence S. Wald, R.N., he studied the treatment of terminally ill patients, which Wald believed was often futile and dehumanizing. Wald told Wessel his role would be to help her understand doctors' thinking. "I can't explain why doctors do what they do," he told her. But he agreed to help. Their work led to the opening of the nation's first hospice, in Connecticut, in 1974.

There he observed that friends and family were quick to comfort a surviving spouse. "Nobody paid attention to the children," he said. Wessel now writes about childhood grief and has worked in schools, dealing with everything from the loss of a beloved teacher to the loss of the class guinea pig.



Morris Wessel took a broad view of his role as a pediatrician—one marked by involvement in the lives of families.

Wessel retired in 1993, as did LaCamera three years later. Their New Haven practice moved to the suburbs, though their successors were adamant about being on a bus line so that innercity patients would have access. Wessel works two days a week at the Clifford W. Beers Child Guidance Clinic in New Haven.

Wessel's daughter, Lois A. Wessel, R.N., M.S., a nurse practitioner working with underserved patients, said that both her father and mother, Irmgard Wessel, M.S.W., influenced her career. They "went out on a limb to help people have better lives," by addressing issues, such as housing, that are not usually the province of a physician. But her parents were not grim saints. "They clearly enjoyed what they did and were very committed to it," she said. As she accompanied them around the city, she saw patients and clients light up. "They were loved and liked and respected." Upon his retirement, hundreds of people gathered in New Haven's Edgerton Park for "Morris Wessel Day."

With HMOS mandating shorter visits and with greater technical expertise expected of physicians, Wessel worries that pediatricians are discouraged from knowing their patients as deeply as he did. "There was something about our practice that was unique," he said. "But it should not be unique at all."

—Colleen Shaddox

Tap dancing through medicine, from surgeon to song-and-dance man

While a medical student at Yale, **Brock Lynch**, M.D. '47, sang and tap danced in a hospital fund-raising play. He remembers thinking, "Should I be in show business or medicine?" But even though he'd started tap dancing when he was 8, Lynch wasn't serious about changing careers. After World War II Navy service, he resumed his medical career and decided that someday he would return to the stage.

And he has. Since he retired in 1995 from practicing general medicine at the Northampton VA Medical Center in Leeds, Mass., he has been part of Young@Heart Chorus, a Massachusetts performing troupe, in which the average age is 80. Other men and women who sing in the group were engineers, insurance executives, building contractors and teachers in their younger days. Rather than croon Cole Porter songs or others of the same vintage, the 73to 91-year-olds sing tunes from the Rolling Stones, Bruce Springsteen, U2, the Beatles, Jimi Hendrix, Led Zeppelin and the Clash—the same loud music that they once told their children to turn down.

In the last seven years, the 22member group has toured Europe 10 times and visited Hawaii and Australia. Lynch sings tenor and dances, although there's not much demand for tap when



Brock Lynch, left, sings and dances with the Massachusetts-based Young@Heart Chorus, which specializes in classic rock.

you've got an electric guitar and professional drum set. Young@Heart plays to sold-out audiences in Europe; in 2001, the King and Queen of Norway gave them a standing ovation.

Because of their age, choice of music and humorous and whimsical performances, last June they were written up in *Time* magazine. The group disco dances to the Bee Gees' "Staying Alive," and Lynch is one of three soloists in "Once in a Lifetime," originally sung by the Talking Heads.

When they go abroad once a year, for a week or two, Young@Heart members face a grueling schedule, usually one performance each night over four nights. This fall, they traveled to London for two weeks, where the group performed 12 straight shows, including a matinee and evening event on a Saturday. These performances come after long plane rides and jet lag. (They always travel with three wheelchairs just in case.) The group pays tribute to each country it visits, so it may learn a song in Dutch while in Antwerp or perform Olivia Newton-John's "Let's Get Physical" in Australia.

Back in Northampton, there are weekly rehearsals, sometimes more, where Lynch and fellow members stand for two hours straight. That's a feat for anyone, but particularly for septuagenarians, octogenarians and nonagenarians whose collective conditions include arthritis, heart disease, macular degeneration, hip replacements, high blood pressure and cancer. (There are chairs at the back of the stage for anyone who gets tired.) Lynch, who jogs three times a week for 10 minutes, doesn't complain about the pace, however. "Young@Heart puts a schedule into my life," said the 81-year-old, "and without it I'd be in a rocking chair."

These days, the only rocking Lynch does is on the dance floor. But that's nothing new. Everywhere he studied or practiced medicine, he would tap dance and sing in charity hospital shows. After his New Haven theatrical debut, Lynch performed during a surgical internship at the University of Cleveland Hospital and his residency at Malden Hospital in his hometown of Malden, Mass., and at New England Medical Center and St. Elizabeth's Hospital in Boston. He tapped his way through Mitchell Air Force Base on Long Island while he was chief of surgery and also when he became a teaching fellow at Memorial Sloan-Kettering Cancer Center.

Then there was more performing while in private practice with his father in Malden for 18 years, followed by more dancing and singing when Lynch moved his work life in 1975 to the Veterans Administration hospital near Northampton as a general practitioner. During the 20 years he practiced there, his surgical skills were frequently requested in the emergency room, leading to the saying, "In a Pinch, Call Lynch."

Within a month of retiring from his VA post in 1995, the self-taught tenor auditioned for Young@Heart. He danced and sang his way through "Button Up Your Overcoat" and "You're the Cream in My Coffee"—a far cry from the rock and roll he would churn out as a group member. "In show business, when you audition, the director always asks what your talent is," said Lynch. "In my case I said, 'For you, I'm a singer who dances, but if you ask me what I really am, I'm a dancer who sings."

He is also a doctor who dances and sings.

—Sally Abrahms

Familiar Faces

Do you have a colleague who is making a difference in medicine or public health or has followed an unusual path since leaving Yale? We'd like to hear about alumni of the School of Medicine, School of Public Health, Physician Associate Program and the medical school's doctoral, fellowship and residency programs. Drop us a line at ymm@yale.edu or write to Faces, Yale Medicine, P.O. Box 7612, New Haven, CT 06519-0612.

Alumni NOTES







Albert W. Diddle, M.D. '36, is pro-

original chair of obstetrics and

at the University of Tennessee

fessor emeritus and was the

gynecology at Memorial **Research Center and Hospital**

in Knoxville. The author or

co-author of 131 publications

gynecology and the history of

medicine, he has also privately

published his memoirs for his

family, U.S. Naval Duty During

World War II: Key West, Florida;

Guadalcanal; Okinawa; Guam;

B. Herold Griffith, M.D. '48, was

elected an honorary member of

the British Association of Plastic

in 1996, is professor emeritus of

plastic surgery at Northwestern

Edward Wasserman, M.D. '45, has

Year 2005 by the Greater Bridge-

port (Conn.) Medical Association

been named Physician of the

for his volunteer work at an

Stephen M. Krant, M.D. '69, HS

in plastic surgery in La Jolla,

'76, has been in private practice

Calif., for 29 years, specializing in

aesthetic and reconstructive sur-

gery. He and his wife, Lyn, have

established the SK Institute,

a nonprofit which sponsors a

monthly Breast Cancer Nite,

where breast cancer survivors

listen to speakers, enjoy food

AmeriCares Free Clinic.

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University School of Medicine.

Surgeons. Griffith, who retired

surgery and chief emeritus of

and Tientsin, China.

1940s

on anatomy, obstetrics and

1980s

Alan B. Astrow, M.D. '80, has been appointed director of the division of hematology/oncology at Maimonides Medical Center in Brooklyn, N.Y. Astrow moved from St. Vincent's Hospital in Manhattan, where he was associate medical director of the cancer center. "We open a 50,000-square-foot state-ofthe-art cancer center this fall," he writes. He is joined at Maimonides by classmate Carl F. Schiff, M.D. '80, who is director of rheumatology.

Robert Hartman, M.D., HS '86, writes to say that he is a clinical associate professor of dermatology at the University of Southern California School of Medicine. In October 2004 he passed a new board exam in pediatric dermatology. For four months each year he heads a pediatric dermatology clinic at Childrens Hospital in Los Angeles.

Reginald J. Sanders, M.D. '85, HS '86, chief of the retinal service at the Georgetown University/Washington National Eye Center, was named one of the top physicians in the Washington, D.C., metro area by Washingtonian magazine in July. Sanders also serves on the board of the American Society of Retina Specialists.



Krystn R. Wagner, PH.D. '89, M.D. '96, assistant professor of medicine (infectious diseases/AIDS program) at the School of Medicine, and José F. Salvana, M.D., an infectious disease specialist, were married in May in Baltimore. Wagner is the medical director of the Nathan Smith HIV clinic at Yale-New Haven Hospital. Salvana is the HIV clinical director at the Hill Health Center, a community clinic in New Haven.

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Alison L. Days, M.D. '99, and Sergio Rico Jr., M.B.A., were married in Cancún, Mexico, in February. Days is a pediatrician at Texas Tech University in El Paso, and her husband is a maintenance supervisor at Penske Truck Leasing.

Mauricio J. Garrido, M.D. '98, a cardiothoracic surgery fellow at **Columbia University Medical** Center in New York, and Louisa Terry, an executive director of the Ovarian Cancer Research Fund, a nonprofit agency in New York, were married on April 9 in Miami.

Steven M. Kawut, M.D. '95, the Herbert Irving Assistant Professor of Clinical Medicine in Epidemiology at the Columbia University College of Physicians and Surgeons, and Elizabeth S. Platzker, a senior designer at Liz Claiborne, the clothing and accessories company, were married on May 29 in Los Angeles. Kawut teaches and conducts research on pulmonary hypertension and lung transplantation.



Herold Griffith

Stephen Krant

Lloyd Friedman

Robert Hartman



and beverages and receive free spa treatments at the SK Sanctuary, which is affiliated with Krant's practice. The institute also holds melanoma, prostate and ovarian/uterine

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cancer nights.

Lloyd N. Friedman, M.D. '79, clinical professor of medicine at the School of Medicine, received a grant from the National Institute for Occupational Safety and Health to study new gamma interferon assays in the diagnosis of latent tuberculosis. In April he received the David Lyman Russell Award from the Connecticut chapter of the American Lung Association for contributions to the prevention and treatment of tuberculosis. Friedman is the vice president of medical affairs and the medical director of Intensive Care and Respiratory Therapy at Milford (Conn.) Hospital.

Robert H. Posteraro, M.D. '73, HS '78, FW '79, a radiologist with Lubbock Diagnostic Radiology in Texas, graduated from Oregon Health & Science University with a master of biomedical informatics degree in June.

Eddie Reed, M.D. '79, has been named the director of the Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion at the Centers for Disease Control and Prevention. He started his new position in June. Reed previously worked at the National Cancer Institute and at The Mary Babb Randolph Cancer Center at West Virginia University.

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Zimra Gordon

James Moore

Andrea Pernack, M.P.H. '98, a program officer at the Institute of Medicine, and Dean Anason were married on May 1, 2004, in Warren, Mich. Pernack, now Pernack-Anason, has worked on studies involving the national smallpox vaccination program and data sharing for a vaccine safety research database.

Lynn E. Sullivan, M.D. '96, HS '00, was married to David A. Fiellin, M.D., HS '95, FW '97, in September in South Salem, N.Y. Sullivan is an assistant professor of medicine at the School of Medicine, where Fiellin is an associate professor of medicine.

2000s

Cristina Baseggio, M.D. '05, was married in May to Seth Alexander, a director of investments in the office of the Yale Endowment. Baseggio began a residency in internal medicine at Brigham and Women's Hospital in Boston in June.

Jonathan Solomon Erulkar, M.D. '01, and Deirdre "Dede" Holden Carroll, M.S.N. '00, A.P.R.N., were married on August 1, 2004, in Lake Forest, III. Fellow Yale Medicine grads who attended included John Abraham, M.D. '00, and Badri Rengarajan, M.D. '99. Erulkar is in his fifth year and a chief resident in the Department of Orthopaedic Surgery and Rehabilitation at Yale. Carroll, a psychiatric clinical nurse specialist and adult nurse practitioner, is a third-year PH.D. student at Boston College. Previously she spent several years as a co-investigator in the Clinical Trials Program at the Yale Child Study Center and on the clinical faculty of the Yale School of Nursing. Since their honeymoon on Anguilla, the newlyweds have settled into married life in Branford, Conn. In 2006, however, they will be moving to Boston, where Jonathan has accepted a spine surgery fellowship at the New England Baptist Hospital and a clinical faculty appointment with Tufts University School of Medicine.

Zimra J. Gordon, M.P.H. '02, D.V.M., and Steven J. Danzer, PH.D., were married on April 17. Gordon is a veterinarian at the Rippowam Animal Hospital in Stamford, Conn., and a research associate with the Yale Occupational and Environmental Medicine Program. Danzer is an environmental planner for the town of Stratford, Conn.

Elizabeth W. Holt, M.P.H. '05, and Matthew J. Delfino Jr., M.B.A., were married in June in Greenville, S.C. After their honeymoon, the couple moved to Boston, where Delfino is employed at Brigham and Women's Hospital.

Anita Karne, M.D. '02, and Mehul A. Dalal, M.D., M.SC., were married in July in Knoxville, Tenn. Karne is chief resident in primary care at New York University School of Medicine. Dalal is an attending physician in medicine at N.Y.U.-Bellevue Medical Center. Matthew P. Kronman, M.D. '03, was married in September to Evelyn K. Hsu, M.D., in Seattle. They met at Children's Hospital in Seattle, where both were residents in pediatrics.

D. Scott McBride Jr., M.D., HS '05, completed a residency in anesthesiology in June and is now a staff anesthesiologist with the U.S. Air Force at Elmendorf Air Force Base near Anchorage, Alaska. He's scheduled to be deployed to Iraq in May 2006 to serve in a field hospital.

James Moore, M.P.H. '03, is one of 10 fellows selected to participate in the newly established Association of Schools of Public Health/Centers for Disease Control and Prevention (CDC) International Global AIDS Fellowship Program. The program is part of CDC's Global AIDS Program, which is part of President Bush's five-year initiative to channel \$15 billion into HIV/AIDS treatment and prevention in 12 African countries and Guyana and Haiti.

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William T. Bachmann, M.D., HS '74, died on July 28 of cancer. He was 65. Bachmann, a dermatologist, lived in Stonington, Conn., and maintained a practice in Westerly, R.I., for more than 30 years. During the Vietnam War Bachmann served as a physician on submarines based in Groton, Conn. He was known in the area not only as a physician, but also for his enthusiasm for fishing for tuna and marlin. In recent years he began exploring area wildlife by boat and kayak. An activist and defender of healthy sea life, he recently completed a book about his fishing experiences and environmental insights.

In memoriam

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Horst N. Bertram, M.D., HS '59, a radiologist, died on March 12 in Cornwall, Pa. A native of Berlin, Germany, Bertram completed his medical studies at the end of World War II, then began a residency in Ohio. After serving as a battalion surgeon in the Army during the Korean War, he came to Yale to complete his residency in radiology. In 1965 he joined the staff of the Good Samaritan Hospital in Lebanon, Pa., where he stayed for 30 years. He served as chair of the radiology department and president of the Lebanon County Medical Society.

Sister Mary Anne Fitzmaurice,

R.N., M.P.H. '69, a member of the Sisters of St. Joseph, died on May 1 in West Hartford, Conn. She was 80. Fitzmaurice received her nursing degree from St. Francis Hospital School of Nursing in Hartford, Conn., and in 1955 became operating room supervisor at St. Mary's Hospital in Waterbury, Conn. In 1967 she began studies in hospital administration at Yale. After her graduation in 1969 she spent a year at the Hospital of St. Raphael in New Haven as a resident in administration. During her career she also worked at St. Francis Hospital in Hartford, the Provincial House of the Sisters of St. Joseph in West Hartford and the Intensive Education Academy in West Hartford. She was honored with a Certificate of Membership in the American College of Hospital Administrators, and in 1979 the mayor of Hartford recognized her service with a Certificate of Award.

Frederick P. Glike, M.D. '41, died on September 12 at his home in Meriden, Conn. He was 89. A lifelong resident of Meriden, Glike graduated from Harvard University before entering the medical school at Yale. During World War II he was a captain with the Third Battalion and participated in the Battle of the Bulge. He returned to Meriden, where he practiced medicine for 40 years until his retirement. Glike loved music and played the clarinet in the Meriden Symphony. He also enjoyed the outdoors and took hiking trips with his family in the White Mountains, where he climbed all peaks over 4,000 feet.

Victor C. Hackney, M.D. '43, died on September 5 in Geary, Okla. He was 88. During World War II Hackney served in the Navy. Board certified in dermatology and pathology, he studied at the Armed Forces Institute of Pathology. He received academic appointments at the University of Southern California and at Stanford University before becoming founding chair of dermatology and professor of dermatology and pathology at Indiana State University School of Medicine. He retired in 1976.

H. David Kearing, M.D., HS '68, died on September 9 at his home in Brackney, Pa. He was 68. After receiving his medical degree from Cornell in New York, Kearing completed a residency in ob/gyn at Yale. He subsequently served in the U.S. Army at West Point for two years. From 1972 to 1991 he practiced ob/gyn in Binghamton, N.Y., with two partners, then went into private practice until 2001, when he retired. Carter Lee Marshall, M.D. '62, M.P.H. '64, died on February 18 in Tucson, Ariz. After service in the Army, Marshall was on the faculty at the University of Kansas School of Medicine, the Mt. Sinai School of Medicine and the City University of New York. In the 1970s he helped set up a medical school at Morehouse College in Atlanta. He later served as director of medical education at the University of Medicine and Dentistry of New Jersey, before moving to Arizona to work at the Health Services Advisory Group, the state's Medicare quality improvement organization. He co-authored an introductory text for allied health workers and published more than 70 articles.

Willys M. Monroe, M.D. '41, a pathologist, died on March 18 in Lynchburg, Va. Monroe was a life fellow of the College of American Pathologists, a fellow of the American Society for Clinical Pathology and a life member of the Medical Society of Virginia. During his career he spent five years in the U.S. Public Health Service, leaving as a lieutenant colonel to become chair of the department of pathology at Richmond Memorial Hospital, where he established a blood bank and trained lab technicians. He also taught pathology at Virginia Commonwealth University and the University of Virginia. He was the first chief of the Richmond Metropolitan Blood Service.



Richard B. Ogrean, M.S. '52, died on June 2 in Fort Myers, Fla. He was 83. After serving in the U.S. Army Medical Corps in Europe during World War II, Ogrean obtained a degree in public health administration at Yale, then worked as an assistant administrator at Yale-New Haven Hospital. In 1956 he became an administrator at Windham Community Memorial Hospital in Willimantic, Conn., where he stayed for 18 years. He worked at other hospitals until his retirement in 1983. He was also a deacon at the First Baptist Church in Willimantic.

Howard Rasmussen, M.D., PH.D., a former professor of medicine and cell biology and chief of endocrinology and metabolism at the School of Medicine, died on April 20 in North Carolina after a long illness. He was 80. Rasmussen was one of the first scientists to recognize the importance of calcium as a signaling molecule. During his career he was chair of biochemistry at the University of Pennsylvania and founding director of the Institute of Molecular Medicine and Genetics at the Medical College of Georgia. Rasmussen was at Yale from 1976 to 1993.

Robert T. Sceery, M.D. '50, died on February 18 of congestive heart failure in Cohasset, Mass. He was 84. Sceery, a pediatrician, was school physician in Cohasset for more than 40 years. Known for his quiet manner, he made house calls and saw patients regardless of their ability to pay. Although retired for several years, Sceery saw occasional patients and attended weekly rounds at Massachusetts General Hospital. During World War II he joined the Navy, piloting a tank landing ship to Normandy beach on D-Day and participating in assaults on southern France and Japan.

Paul W. Sternlof, M.P.H. '57, died in Sharon, Conn., on August 12. He was 73. Sternlof served as assistant administrator of Baltimore General Hospital in Maryland from 1958 until 1962, when he became president of Sharon Hospital. He remained in that post until 1989.

Daniel B. Stryer, M.D. '90, director of the Center for Ouality Improvement and Patient Safety at the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services, died on May 19 in Rockville, Md., of complications from a brain tumor. The center provides information to patients and the health care industry to improve quality of care. Stryer took on his job in 1997, after a residency in internal medicine at the University of California, San Francisco, and,

with his wife, pediatrician Stacy Beller Stryer, M.D. '91, spent three years with the Indian Health Service in Arizona.

George Tyler, M.D. '67, died on August 28 in Bethlehem, Pa. He was 65. Tyler, a fellow of the American College of Surgeons, was a senior surgeon at Lehigh Valley Hospital-Muhlenberg and an instructor for the "Advanced Trauma Life Support" course. He was a major in the U.S. Army Seventh Cavalry and served in Vietnam, where he received the Bronze Star.

Vernon T. "Doc" Watley, M.D. '49, died on August 30 in Beaumont, Texas. He was 83. In March 1942 Watley enlisted in the U.S. Air Force and served at what later became Lackland Air Force Base in Texas. During the Korean War he was called back to duty and ran the neurological service at Lackland. After his military service, he was the superintendent of Abilene State Hospital for Epileptics and a psychiatrist at Austin State Hospital. During his career he was also an emergency room doctor and, until his retirement in 1981, a family physician.

SEND OBITUARY NOTICES TO

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A "perfume" to prevent disease

Early in 1999 John R. Carlson, PH.D., the Eugene Higgins Professor of Molecular, Cellular and Developmental Biology, reported that his laboratory had identified 16 odor receptor genes in fruit flies (See "Researchers Discover Odor Receptor Genes in Fruit Flies," Spring 1999). It was the first finding of such genes in insects. Carlson and his colleagues went on to find taste receptor genes in fruit flies and to identify the functions of specific odor receptors in mosquito antennae.

Now Carlson's laboratory is part of an international team that plans to harness those findings to reduce the spread of malaria, which kills 1 million people each year, mostly in the developing world. The female mosquitoes that spread the disease are drawn to certain human odors, which they "smell" with receptors in their antennae. The team, which includes scientists in the United States, the Netherlands, Tanzania and Gambia, hopes to create a "perfume" that will either lure malaria-carrying mosquitoes into traps or act as a repellent.

Scientists at Yale and Vanderbilt University will identify odors that affect mosquitoes and will create the "perfumes." Dutch researchers will study the effects of the odors on mosquito behavior in the laboratory. And the African scientists will field-test the odors. The \$8.5 million, five-year project is funded by the Bill & Melinda Gates Foundation's Grand Challenges in Global Health initiative. Ultimately, the scientists hope the odors they develop will prevent malarial mosquitoes from infecting humans, and will be inexpensive, safe and easy to use in rural areas. This approach could also be applied to mosquitoes that carry dengue fever or the West Nile virus. "With insect-borne diseases, the best way to control the disease is usually to control the insect," Carlson said. "We smell good to the mosquitoes, so if we can understand in molecular detail how the insects are attracted to us, we might be able to devise new means of controlling them."

—John Curtis

Archives 50 AND 25 YEARS AGO



JANUARY 1955 Alumni Bulletin

Students' Loan Fund of Yale Men in Medicine

"The following statement is published at the request of the officers and incorporators of the Students' Loan Fund of Yale Men in Medicine, Inc.

"It is estimated that it costs a student a minimum of \$2,000 for each of his four years of residence at the Yale University School of Medicine. Although this represents only a fraction of the total cost of his medical education, it is nevertheless a considerable sum. ... In the present academic year, ninety students, or twenty-seven percent of the student body, have requested such help. ...

"The Students' Loan Fund of Yale Men in Medicine has been for twenty years a modest but continuing source of help to our needy and worthy students. Since its inception in 1934, this Fund has provided loans to one hundred and twenty of our students."



SUMMER 1980 Yale Medicine

Human Genetics finds a new home

"The completion of the third floor of the Nathan Smith Building has long been awaited by members of the Department of Human Genetics. 'It seems as though we had outgrown facilities in the LCI building even before we moved in,' a faculty member observed recently.

"During the past two decades, the study of human genetics has become one of the most rapidly advancing and challenging fields in medical science. 'It is hard to believe now, that in the 1950s when I and many of my colleagues were in medical school, human genetics was a relatively minor subject,' Dr. Leon Rosenberg, chairman of the Department, remarked a few years ago.

"The Nathan Smith Building ... symbolizes the spirit in which the Department was founded in 1972. At the time, Dr. Rosenberg stated, 'The fundamental philosophy behind this departmental organization is that the application of basic genetic knowledge to the problems of human illness can best be accomplished in a climate which encourages close interaction between those with expertise is basic laboratory genetic science and those who are concerned with patients with genetic problems. This is a new concept in academic medicine."

TULANE STUDENTS FIND A SAFE HAVEN AT YALE

Dorota Ruszczyk had just returned to New Orleans from fieldwork in Kenya when she learned that Hurricane Katrina was about to land. She and her fiancé stocked up on food, batteries and water, but as the storm approached, they left for Baton Rouge. Now Ruszczyk is with her family in New Haven and finishing her M.P.H. course work at Yale rather than Tulane. Memories of the days after the storm still haunt her. "You saw everyone around you with a blank stare on their face," she said. The hurricane diverted Andrea Humphrey, м.р.н. '05, from a doctoral program at Tulane back to Yale, where her former advisors helped her sign up for course work. Although her clothes, computer and textbooks are in New Orleans, Humphrey considers herself lucky. "It's going to be very hard for people to get their lives back together," she said. David Grew, who was about to enter public health school at Tulane, is taking classes at Yale. He weathered the storm with his landlord's family in Houma, La., then spent time in Texas, including a day helping evacuees in Austin. "It had a real effect on me, in how I look at the way health care should be distributed," said Grew.

Grew, Humphrey and Ruszczyk are among five students from Tulane who have found temporary homes at the medical school after Hurricane Katrina forced the closing of Tulane University in late August. While the public health students are in the classroom, two Tulane medical students are at Yale for clinical clerkships.

The day before Hurricane Katrina struck, fourth-year Conar Fitton left New Orleans with "three T-shirts, a pair of flip-flops and a dog." Stephanie Malliaris, a third-year, had left a day earlier. "Most people leave for hurricanes thinking they'll be back home in three or four days," she said. Fitton spent two weeks at Yale in a hepatology rotation. Malliaris stayed eight weeks for a pediatrics clerkship. In September Tulane relocated its medical school to Houston. Other Tulane programs are expected to resume in January in New Orleans.



Andrea Humphrey, center, who received her M.P.H. from Yale in May, returned to New Haven in September after Hurricane Katrina led to the closing of Tulane University, where she was about to begin doctoral studies. At Yale she took classes and also found work as a teaching assistant.

—John Curtis

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