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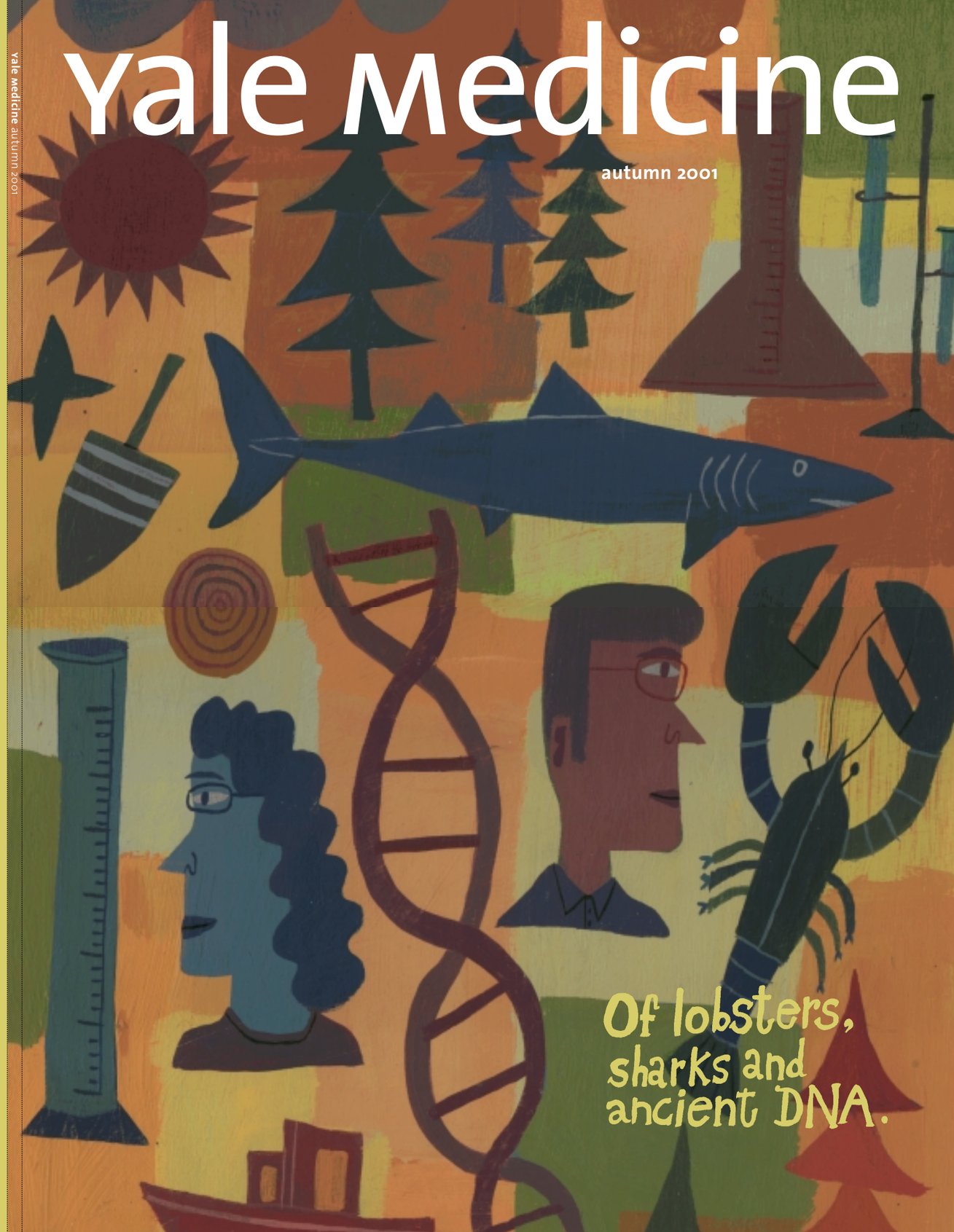

ON THE COVER

A week at the beach or a week at the bench? Science won out for two dozen students who spent part of their summer break in the lab in Maine, but the scenery wasn't bad either. Page 18.

Illustration by Calef Brown

yale Medicine

AUTUMN 2001

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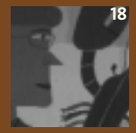
This season on the Web
info.med.yale.edu/ymm

Explore the following topics in greater depth by visiting our website and selecting EXTRAS:

- The Historical Library's online exhibit about the School of Medicine's early 20th century history
- The Mt. Desert Island Marine Biological Laboratory
- The International Health Program
- Additional photos from Alumni Reunion Weekend

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



SHARKS, SALT (AND A TASTE OF LOBSTER)

An intensive week at the bench in Maine introduces students to modern lab strategies and techniques, ancient DNA and a clambake to write home about.

by John Curtis

A WORLD OF DIFFERENCE

Yale's International Health Program sends young doctors around the globe to provide needed care—and learn the basics of a simpler medicine.

by Cathy Shufro

AN EPIDEMIC IN THE MAKING

Type 2 diabetes poses alarming health risks as obesity soars and exercise is crowded from modern life. Yale investigators are seeking better ways to prevent and treat the disease and to understand the science of fat.

by Randi Hutter Epstein

COMMUNICATION STILL DOESN'T COME EASY

I read with interest your article entitled "A Dramatic Turn" [Spring 2001] regarding the physician-patient relationship. I suspect my experience during my tenure at Yale in the early 1980s was fairly typical. I certainly received the message that truly caring about the patient as an individual was very important, but I did not receive any training regarding how to make that "caring" experience happen on any consistent basis.

This article tells me that Yale still cares very much about the patient. But I was disappointed to note its suggestion that Yale still does not know how to teach the student how to make the physician-patient relationship happen within the short appointment reality of primary care today.

I am now one of the chiefs of ophthalmology with Kaiser and The Permanente Medical Group (TPMG) in California. I have also just been recruited to be the local "communication consultant" in our facility. Communication consultants like myself are given training on the essential ingredients of an effective patient-provider interaction. These evidence-based elements have been dubbed the "Four Habits of the Highly Effective Clinician." They form the backbone of an eight-hour curriculum which teaches the participants four key skills that allow the physician to make a satisfying human connection with the patient—even within a 15-minute interaction.

Awareness-building presentations like those of Ms. Smith's are highly valuable. I think the next step might be offering our physicians-in-training a program similar to TPMG's, one that teaches specific and achievable techniques to improve communication.

ELLEN KOLARIK, M.D. '85
PETALUMA, CALIF.

TAKING THE PULSE OF HEALTH INTERACTIONS

In the Spring 2001 issue, the article "A Dramatic Turn" provided a thought-provoking look at the physician-patient relationship. We want to call your attention to another Yale-based initiative that examines the clinician-patient relationship.

The Program for the Study of Health Care Relationships, funded by the Patrick and Catherine Weldon Donaghue Medical Research Foundation, is a collaborative project between Yale University and the University of Connecticut. The program's mission is to bring issues surrounding the relational aspects of care to the forefront of the ongoing discourse about health care in Connecticut and the nation. It seeks to enable patients, health-care professionals, providers, health policymakers and other interested individuals to engage in successful partnerships, with the shared goal of improving patient outcomes, especially in the context of adherence to therapeutic regimes.

A multidisciplinary team has been working for a year to study the relational aspects of care and their effects on adherence. The interdisciplinary program provides a forum for a range of issues, including health education; the role of the Internet and technology; the influence of organizations, insurance and policy; and the relationships among professions, as well as with patients. The group consists of physicians, nurses, social workers, consumers, academics and others, and has a website: info.med.yale.edu/nursing/hcr/ .

SALLY COHEN, R.N., PH.D., DIRECTOR, PROGRAM FOR THE STUDY OF HEALTH CARE RELATIONSHIPS; ASSOCIATE PROFESSOR, YALE SCHOOL OF NURSING

THANK YOU FOR AN OUTSTANDING MAGAZINE

May I take this opportunity to commend you on the excellent quality and caliber of *Yale Medicine*. It is outstanding, informative, insightful and pleasurable to read. Thank you for your superior effort.

LEE H. STROHL, M.D. '68
LAKESIDE, MICH.

The current format of *Yale Medicine* is terrific. It is global in its perspective, clearly informative and upbeat. Your accomplishment as well as the accomplishments of those featured rekindles the pride we all shared in YSM when we fledged various decades ago. Thank you for your efforts. I have begun looking forward greatly to successive issues.

GLENN L. KELLY, M.D. '62, HS '66
ENGLEWOOD, COLO.

WHAT THE STORY SAID ABOUT NEEDLE EXCHANGE

I was very much impressed by "What the Needles Said" [Summer 2001]. This very positive and accurate reporting of the events that led to the creation and successful implementation of New Haven's Needle Exchange Program is perhaps the best summary of the program that I have seen.

The Yale medical community deserves a great deal of gratitude for its support of needle exchange at a time when the entire nation was still very much in a "black death/bubonic plague" panic in regard to AIDS. I'm proud that my city and my police department proved positive in rising to the challenges which were thrust upon us at that moment in history.

NICHOLAS PASTORE, DIRECTOR, CRIMINAL JUSTICE POLICY FELLOWSHIP; FORMER CHIEF OF POLICE, NEW HAVEN, CONN.

HOW TO REACH US

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

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FROM THE EDITOR

Walking a fine line

Every so often someone will offer an idea for an article or a comment about a piece they read in "the journal," meaning *Yale Medicine*. Along with my thanks, I usually note that *Yale Medicine* is more journalism than journal, a magazine rather than a medical tome. This is an important distinction in academia, where the peer-reviewed scrutiny and serious aims of scientific publishing reflect one set of core values.

We're a slightly different animal. Our primary goal is to keep alumni in touch with each other and informed about the work and scholarship that goes on here. Our objective is to be intriguing to a wide audience and still relevant to each of our readers, whose interests run the gamut from structural biology to the history of medicine. As cartoonist Sidney Harris observes below, what one subspecialist finds hopelessly general may be incomprehensible to another learned person. It is our intent to bridge that gap in a way that readers will find engaging.

We hope you'll let us know how we're doing. As this issue went to press, we received some welcome feedback from the Association of American Medical Colleges, which honored *Yale Medicine* with its highest level of recognition, the Award of Excellence. Also this issue, we are completing the final phase of the magazine's redesign. I appreciate the suggestions we've received along the way and hope you like the result.

Michael Fitzsousa
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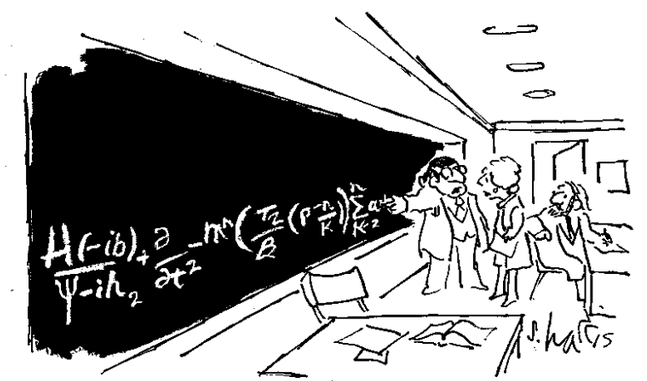


MICHAEL MARSLAND

Students placed candles around the rim of the Women's Table on Cross Campus during a vigil the evening of September 11. Hundreds of people from throughout the Yale community gathered to honor the victims of the day's tragedies.

"THE STRANGEST KIND OF LETDOWN"

On September's day of terror, Yale geared up to treat survivors who never came.

On September 11, a day of death and panic elsewhere, there was an odd sort of quiet in New Haven. In the medical school's clinics and classrooms, the day's routine activities fell by the wayside, overwhelmed by the horror of what was happening in New York, Virginia and Pennsylvania. The medical center geared up for an onslaught of trauma cases that never materialized. For 24 hours, Yale-New Haven Hospital was on disaster alert for survivors who might have been pulled from the wreckage of the collapsed World Trade Center only 90 miles away. But, said a hospital spokeswoman, "It was the strangest kind of letdown. There were no patients to help."

Medical school faculty and alumni who provided aid in Lower Manhattan experienced a similar disappointment. Emergency physician Scott Weir, *m.d.*, a veteran of search-and-rescue efforts including the 1998 bombing of the U.S. embassy in Nairobi, had never seen anything like the devastation at the World Trade Center. During a week on the scene he treated no survivors, only rescuers with minor injuries. Kenneth C. Rondello, *m.p.h.* '94, *m.d.*, spent four days at the blast site and Chelsea Piers, where an ice rink became a morgue and the set of television's "Spin City" a trauma center. "No news footage you've seen or descriptions you've heard can truly do it justice," he said. "The air was permeated with the nauseating, acrid smell of burning jet fuel. Everything was covered in inches of gray ash, as if a volcano had erupted."

Life went on at Yale but the tragedy haunted everything that followed. No gathering could begin without some acknowledgement of "the events of September 11." The day of the attacks, classes were canceled for first- and second-year medical students, some of whom traveled to New York to volunteer in the Office of the Chief Medical Examiner. That first night, hundreds of students and faculty members carried candles down College Street to a vigil at Cross Campus.

In the days that followed, the University responded with drives for blood and donations, along with lectures and discussions on terrorism, foreign policy and Islam. Students at the School of Public Health held a teach-in. Medical and public health students visited local merchants of Middle Eastern descent to reassure them at a time when they might fear discrimination. On September 28, speakers invited by the Department of Psychiatry and the Child Study Center explored the ways in which people cope with a world turned upside down.

Among those determined to get on with their lives were Edwin Thrower, *ph.d.*, a postdoctoral associate in the Department of Pharmacology, and his fiancée, Bozena Sakowska. They decided to go ahead with their wedding September 15, even though his parents and friends in England could attend only via a conference call. The ceremony included a prayer for victims of the attacks, and ended on an upbeat note. "We had friends come from Manhattan," Thrower said. "They said this was very much needed—a celebration of joy, love and life."

STEM CELL SCIENTIST URGES CONGRESS TO FUND EMBRYONIC RESEARCH

When Diane Krause, *m.d.*, *ph.d.*, published findings this spring from her work on adult-derived stem cells in mice, she didn't expect to become a player in a national political debate. "I thought it would be important for those of us in the field," she said in July, adding "I didn't realize it was going to get such press attention."

Krause, an associate professor of laboratory medicine and pathology, identified adult stem cells in bone marrow that can also create new liver, lung, gastrointestinal and skin cells. Working with collaborators at Johns Hopkins and New York University, she found the first evidence that these progenitor cells are capable of creating up to 15 different mature cell types (See *Findings*, page 13).

Since the publication of her work in the May issue of *Cell*, Krause has been besieged by media inquiries from around the world. In early summer, she was asked to testify on Capitol Hill.

Her conclusions were published as the national debate over embryonic stem cell research was heating up and, to her dismay, have provided fodder to opponents of such work, which requires the destruction of human embryos. Those who oppose embryonic stem cell research for moral reasons argue that it is unnecessary because adult stem cell research shows such promise. Krause insists that research down both avenues is vital.

In July she had a chance to make her point before the U.S. Senate Appropriations Subcommittee on Labor, Health and Human Services and Education, which held hearings on the federal government's role in funding future embryonic stem cell research.

Embryonic stem cell research needs to be funded for three reasons, Krause told the subcommittee. First, these cells can be grown *in vitro*, unlike adult stem cells. Second, because they are the most versatile cells available, embryonic stem cells yield far more information on how they maintain that versatility than adult-derived cells. And third, she said, "No one can predict which lines of investigation will lead to effective and safe treatments for human disease."

On August 9 President Bush outlined his plan for funding embryonic stem cell research: only existing lines of embryonic stem cells, left over from *in vitro* fertilization, could be used in federally funded research. Research using embryonic stem cell lines developed after August 9 would be ineligible for funding. On August 27, the National Institutes of Health released a list of 64 eligible embryonic stem cell lines.

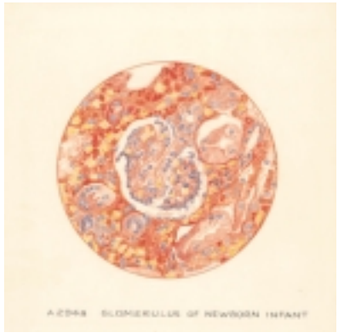
Scientists have questioned that list, noting that many cell lines are unavailable or inappropriate for a variety of reasons.

"The president's plan is not well thought out," Krause said. "It doesn't give federally funded scientists the freedom to pursue scientific questions."

On September 5, Secretary of Health and Human Services Tommy Thompson told a Senate committee that only about 24 of the 64 cell lines were ready for use in experiments. The usefulness of the remaining cell lines, he said, remains to be proven.

FRANK POOLE

In testimony before a Senate subcommittee, Diane Krause urged that federal funding be provided to support embryonic stem cell research. Krause also took exception to the use of her findings on adult stem cells to argue for restrictions on embryonic stem cell funding.



DEPARTMENT OF PATHOLOGY

Armin Hemberger had "an incredible ability to summarize the essence of the anatomical findings of a given condition in a single illustration."

FROM THE AUTOPSY SUITE, A TREASURE TROVE OF "POST-MORTEMISM"

Before photography became the standard for capturing images of important anatomical findings, pathology departments hired specially trained illustrators to create visual materials for teaching and recording medical knowledge. One of the most gifted among them was Armin Bismark Hemberger, whose career at Yale spanned six decades.

Hemberger, who lived from 1896 to 1974, is the subject of new interest and may someday be featured in a documentary film and traveling exhibit.

A student of Max Brödel, who is widely regarded as the father of American medical illustration, Hemberger worked in the tradition of Vesalius, da Vinci and Dürer, combining artistic skill with a remarkable level of scientific accuracy to produce brilliant images in pen and ink, pencil, gouache and watercolor. Approximately 700 of these drawings are preserved in the illustration collection of the Department of Pathology.

"Hemberger was one of the best," said Ranice W. Crosby, director emerita of the Department of Art as Applied to Medicine at Johns Hopkins, where Brödel's papers are archived.

Born in Scranton, Pa., on April 1, 1896, Hemberger graduated from the Maryland Institute of Art and Design in Baltimore. In 1917, he was recruited by Milton C. Winternitz, *m.d.*, as a medical illustrator for the New Haven Station of the Army Chemical Warfare Service. His drawings are in two classic monographs edited by Winternitz, *Collected Studies on the Pathology of War Gas Poisoning* and *The Pathology of Influenza.* Hemberger returned to Baltimore in 1920 for a year of study with Brödel before spending the remainder of his career at Yale. He retired in 1962.

In addition to his medical work, Hemberger painted landscapes and is represented in the collection of the Metropolitan Museum of Art in New York.

In 1987, during the construction of a new autopsy suite, faculty member Raymond Yesner, *m.d.*, noticed two large filing cabinets that had been pushed into the old dissection room. "I was absolutely knocked over by what I saw—hundreds of Hemberger's paintings and drawings stacked one on top of the other." An e=ort to catalog the images began in earnest and steps to preserve the original works followed. Five years ago, Jon S. Morrow, *ph.d.* '74, *m.d.* '76, *hs* '77, chair of the Department of Pathology, asked Katherine Henderson, the department's photography and graphics manager, to begin digitizing the illustrations and transferring the original works into acid-free, archival containers. Working with Deborah Dillon, *m.d.* '92, a faculty member who provided annotation for many of the drawings, this task has now been largely completed.

Last year, Judith Hokanson Barbeau, a public relations consultant hired by the department, saw a stack of Hemberger's art on a shelf and became interested in his life and career. She located the artist's son in New Hampshire, where she examined Hemberger's original watercolors, oils, woodcarvings and engravings. She later located and interviewed Hemberger's former students and colleagues, recording information and personal remembrances.

Hemberger's work has guided generations of medical students and physicians-in-training. One of them was Morrow, who said that the artist "had an incredible ability to summarize the essence of the anatomical findings of a given condition in a single illustration. Hemberger conveys more information about a disease process in a single drawing than a pathologist can assimilate by seeing a dozen examples in dissection."

With the support of Yesner and Morrow, Barbeau hopes to make a film about Hemberger, as well as organize an accompanying touring exhibition of his work.

GRADUATE PROGRAM FOSTERS AN INTERDISCIPLINARY SPIRIT AND A JUMP IN APPLICATIONS

How does an academic program go from newborn to campus fixture in only five years?

Yale's Combined Program in the Biological and Biomedical Sciences (*bbs*) has accomplished this feat by uniting 11 academic departments and fostering a sense of community that's evident from the lab bench to the pages of its irreverent student magazine.

Founded on the principle that research is inherently interdisciplinary and no longer conforms to traditional departmental boundaries, *bbs* provides graduate students with flexible opportunities to study with more than 200 faculty members from across Yale. "There's a lot more interchange than there ever was before *bbs*," said Lynn Cooley, *ph.d.*, the program's new director and a professor of genetics and cell biology. "There's more communication, more coordination, and fewer territorial disputes over resources."

The program is divided into eight interest-based tracks: Biological Sciences, Cell Biology and Molecular Physiology, Genetics and Development, Immunology, Microbiology, Molecular Biophysics and Biochemistry, Neuroscience, and Pharmacological Sciences and Molecular Medicine, each of which draws its faculty from multiple departments. While students affiliate with a single track, they have almost unlimited research opportunities at Yale, including access to faculty in departments such as Computer Science, Engineering, Psychology and Chemistry. *bbs* students "can rotate anywhere and settle into the lab that's most suited to their interests," said *bbs* Administrative Director John Alvaro, *ph.d.* "They have a nice home base and yet they have access to all the labs on campus."

bbs, which streamlined the admissions process and administrative structure for graduate students in the life sciences, has also succeeded in recruiting students. Applications jumped nearly 20 percent in the past year.

One cornerstone of the program's strength has been its partnership with Bristol-Myers Squibb (*bms*), which helped establish *bbs* with a multimillion-dollar grant in 1996. *bms* funds graduate study and provides opportunities for students to gain experience in pharmaceutical research at its Wallingford, Conn., facility.

One of Cooley's priorities is to expand partnerships between life sciences companies and *bbs*. She also plans to embark on a major fund-raising effort to establish an endowment supporting graduate education. And she wants to continue to encourage collaborative research in emerging disciplines such as bioinformatics. The *bbs* program, says Cooley, provides "a way for the campus to nurture new emerging scientific disciplines."

FRANK POOLE

John Alvaro and Lynn Cooley

et cetera

APPLICATIONS HIT AN ONLINE SNAG

Every alum knows about the Yale System of Medical Education and its emphasis on independent scholarship over class rankings, grades and exams. This summer, applicants to the medical school became familiar with a different kind of Yale system, created after the failure of a Web-based application process introduced by the American Medical College Application Service (AMCAS). Technical glitches made it difficult for many applicants to file online, and the system for transmitting application data to medical schools has been crippled by software problems. Unfortunately, the old AMCAS paper-based system had already been dismantled, and medical schools found themselves scrambling to devise new procedures.

The transition system developed by the Admissions Office and the school's information technology staff has worked so well that it has been adapted for use by other medical schools. Despite the problems with AMCAS and a downward trend in medical school applications nationally, applications to Yale have remained steady, according to Director of Admissions Richard A. Silverman. Meanwhile, AMCAS has developed an interim system of its own, sending printed copies of its applications to medical schools via overnight mail. AMCAS has also announced changes in leadership and is devoting substantial resources to evaluating this year's problems while working on a solution for next year.

CONTRIBUTIONS REACH NEW HIGH

For the second year in a row, gifts to the medical school have soared. At the close of fiscal year 2001, philanthropy from all sources totaled nearly $77 million, compared to $63.5 million for the previous year and $40 million in fiscal 1999. Gifts from individuals more than doubled over the past year, from $15.5 million to $33 million. Of particular note was record-breaking giving by reunion classes that celebrated last June. Donations from professional foundations totaled $21 million; private agencies gave just under $16 million and corporations gave $6 million. "These totals are not only a reflection of the generosity of the many friends of the School of Medicine," said Dean David A. Kessler, M.D., "but also a continuing commitment and support for faculty research and clinical excellence."

FRANK POOLE

Marc Potenza has used functional magnetic resonance imaging to localize brain activity associated with pathological gambling to the anterior cingulate cortex.

SLOT MACHINES AND THE CINGULATE CORTEX

The neurobiology of pathological gambling bears striking similarities to that of drug craving.

From the green towers of the world's largest casino rising up from the Connecticut farmland to the smash-hit television program *Who Wants to Be a Millionaire*, a culture that promotes and glorifies gambling is all around us.

But until recently, little has been done to investigate gambling addiction, a significant health problem that may be as prevalent as some other major psychiatric illnesses such as schizophrenia, according to Marc N. Potenza, *ph.d.* '93, *m.d.* '94, an assistant professor of psychiatry and director of the Problem Gambling Clinic at Yale.

Research suggests a rise in the rate of pathological gambling during the explosive growth of legalized gambling in the United States, which began with state lottery systems in the 1960s, proliferated with riverboat gambling and casinos on Native American reservations two decades later, and now continues to expand with Internet gambling and video poker.

While historically viewed simply as a sin or vice, pathological gambling has symptoms similar to those of drug addiction, said Potenza, who is using brain imaging and drug trials to better understand its causes and to develop more e=ective treatments.

"The gambling industry is huge," he said. The $51 billion generated from casinos, lotteries and horse race betting exceeds the revenues of the movie, theme park and music industries combined. One estimate pegs the societal cost of problem gambling—including legal fees for divorces and incarceration, as well as health bills—at $5 billion a year. Potenza believes the price could run far higher.

While it is estimated that 86 percent of adults have gambled at some point in their lives, fewer than 10 percent develop a problem and fewer than 3 percent of those become pathological gamblers, he said. Still, many compulsive gamblers report devastating troubles—their lives torn apart by bankruptcy, divorce and criminal activity. About a fifth of pathological gamblers attempt suicide.

Problem and pathological gamblers, though, have had few treatment options available. For example, about 85 percent of callers to the Connecticut Council on Problem Gambling's hotline reported never having received any prior help for a gambling problem. Potenza is working to change that.

The Problem Gambling Clinic, a collaboration between Yale's Department of Psychiatry and the Connecticut Mental Heath Center, is one of only four sites in the U.S. to participate in the first multicenter trial of a drug to treat compulsive gambling. Initial data from the trial evaluating the effects of paroxetine (Paxil) are encouraging, said Potenza. He is also using functional magnetic resonance imaging to monitor the brain activity of both gamblers and healthy subjects who have viewed videotaped cues intended to spark the urge to gamble. Only in the pathological gamblers did viewing the cues lead to lower activity in the anterior cingulate cortex, a brain region which has been repeatedly implicated in previous studies of drug craving and mood states. While further study is needed, the neuroimaging study may help identify a possible intervention point for patients with the addiction.

MULTIPLE SCLEROSIS THE TARGET OF EXPERIMENTAL SCHWANN CELL TRANSPLANT

Physicians and researchers are hoping that cells from a nerve in a patient's ankle will stem the degeneration of the nervous system caused by multiple sclerosis.

In July a Yale team transplanted Schwann cells from the sural nerve into a patient's brain in an e=ort to reverse the stripping away of myelin, the protective sheath that surrounds nerve fibers in the spinal cord and brain. It was the first central nervous system transplantation to repair the myelin-forming cells in a patient with multiple sclerosis.

"The purpose of this experiment was to determine whether the procedure is safe and has enough promise to justify future research," said Timothy Vollmer, *m.d.*, associate professor of neurology and principal investigator on the experiment.

Animal studies have found that Schwann cells, which make myelin in peripheral nerves, can replace oligodendrocytes, which make myelin in the brain and spinal cord. Vollmer and his team wanted to determine whether Schwann cells can not only survive in the human brain, but also wrap myelin around nerve fibers and restore normal function.

Over two days in July Vollmer's team first isolated Schwann cells from the sural nerve in the patient's ankle. Then, a neurosurgery team led by Dennis D. Spencer, *m.d.*, *hs* '76, used a magnetic resonance imaging machine to guide a needle through the patient's frontal lobe and inject the cells into a previously identified multiple sclerosis lesion. For the next six months researchers will monitor the patient with both neuroimaging and functional assessments. Then surgeons will perform a biopsy to see whether the cells survived and made myelin.

The team included Je=rey D. Kocsis, *ph.d.*, Stephen G. Waxman, *m.d.*, *ph.d.*, and others. The research is funded by The Myelin Project in Washington, D.C.

HOME MONITORS DEEMED INADEQUATE FOR SPOTTING SIDS

Events that home monitors routinely detect as warning signs for sudden infant death syndrome (*sids*), such as a prolonged cessation of breathing or a slow heart rate, may be common even in healthy infants, according to Yale researchers. "This study calls into question the utility of home monitoring for *sids*," said George Lister, *m.d.* '73, *hs* '75, professor of pediatrics and anesthesiology. The findings were published in March in *jama: The Journal of the American Medical Association*.

A study group made up of physicians at institutions around the country monitored 1,079 infants, some healthy and others considered at high risk for *sids*, for periods ranging from 16 to 66 weeks. Infants who were born prematurely, had a sibling who died of *sids* or had experienced a life-threatening event that required intervention were classified as high risk. "The threshold for an 'event' conventionally used for home monitoring picked up so many infants that it would be hard to separate those who are normal and not normal," said Lister, who chaired the study group. Researchers then used special monitors to record breathing and heart rate patterns around the time of an "event."

The most extreme events, those that lasted a very long time by usual medical standards, were common only in infants born prematurely, but occurred before the age when *sids* was prevalent. The study group concluded, therefore, that extreme events are not immediate precursors to *sids*. "These early events might be markers of vulnerability to *sids*," said Lister, "but are unlikely to be events that directly evolve into *sids*."

JAMES YANG

An algorithm developed by Ray Bahado-Singh and Joshua Copel uses data from ultrasounds and other measurements to gauge the risk of Down syndrome.

INSTEAD OF A NEEDLE, SIMPLE MEASUREMENTS RULE OUT DOWN SYNDROME

Yale researchers have developed an algorithm that allows physicians to gauge the risk of Down syndrome in fetuses without resorting to amniocentesis, an invasive procedure that could cause a miscarriage. Instead, physicians rely on what is called an ultrasonic biometry algorithm, which measures risk based on a number of factors, including information gathered by ultrasound—measurements of the fetus's upper arm and skin at the back of the neck.

In a study published in the May issue of the *American Journal of Obstetrics and Gynecology*, Ray O. Bahado-Singh, *m.d.*, associate professor of obstetrics and gynecology, reported that the algorithm proved accurate in almost 80 percent of cases. Having this assessment allows parents to determine whether to proceed with amniocentesis.

Down syndrome is a congenital disorder caused by an extra chromosome 21. Children a=ected have mild to moderate mental retardation, shorter stature and flattened facial features. Women over 35 have a higher risk of giving birth to a child with Down syndrome, but using age alone physicians detect only about one in five cases, said co-author Joshua A. Copel, *m.d.*, professor of obstetrics and gynecology and pediatrics. "Using blood tests and ultrasound we apply adjustments to the mother's age-related risk," Copel said. "This would mean fewer amniocenteses and a higher percentage of abnormal babies identified."

PATHOLOGISTS SET NEW CRITERIA FOR CANCER PRECURSOR

Pathologists tracking the progression of disease from acid reflux to esophageal inflammation to Barrett's esophagus, a precursor of cancer, can't always agree on how to evaluate biopsies. Now, a national group of gastrointestinal pathologists founded by a Yale professor has developed new criteria for grading premalignant changes in cells, also referred to as dysplasia.

Criteria for grading dysplasia were established in 1988, but still led to inconsistent results among pathologists. "That grading decision," said Marie E. Robert, *m.d.*, associate professor of pathology, "is made by looking through a microscope at a slide of a biopsy. It is very subjective."

Using their new criteria, Robert and 11 other gastrointestinal pathologists found that they agreed more often on categorizing dysplasia. Among the revisions they suggested was more attention to the location of atypical cells. Atypical epithelial cells on the surface of the mucosa are more predictive of future cancer than cells in the deep mucosa. The new criteria also sought to clarify the di=erence between low-grade dysplasia, which requires routine follow-up, and high-grade dysplasia, which usually prompts surgical resection, Robert said.

A follow-up study of patients found a correlation between diagnoses with the new criteria and cancer risk. "When we modified and discussed the criteria, the risk of developing cancer went up in a linear fashion, after earlier biopsy diagnoses of negative, low-grade and high-grade dsyplasia," Robert said. "That would argue that our new criteria are valid and can guide clinicians and patients on how they ought to be followed once these diagnoses are made."

The Gastrointestinal Pathology Study Group, which included pathologists from Johns Hopkins University, the University of Michigan, Vanderbilt University and others, published their findings in April in *Human Pathology*.

JOBS AND BRAIN CANCER MAY BE LINKED

Farm workers, waitresses and people who work with rubber or cleaning chemicals are at a higher risk for brain cancer, according to a study by Yale scientists published this spring in the journal *Occupational and E*

JOHN CURTIS

et cetera

TARGETING MACULAR DEGENERATION

Macular degeneration, caused by the deterioration of the central portion of the retina called the macula, affects an estimated one-third of the over-65 population. Now, with a $1 million gift from Foresight Inc. and $1 million in matching funds raised by Yale, the Department of Ophthalmology and Visual Science is on its way to establishing a center to address problems in retinal functioning. The funding will be put toward the $5 million cost of establishing a center to study the cellular and molecular biology and physiology of the development of the retina.

Foresight Inc. is a Connecticut-based charitable foundation. It was founded in 1968 by patients treated by Yale ophthalmologists.

SLEEP APNEA AND STROKE

People who snore, sleep restlessly and feel tired during the day are at higher risk of suffering a stroke, according to a study by a Yale researcher published in the June issue of the journal *Stroke*. "Sleep-related breathing disorders are strongly associated with increased risk of stroke independent of known risk factors," said Vahid Mohsenin, M.D., director of the Yale Center for Sleep Disorders and principal investigator of the study. "Since sleep-related breathing disorders are treatable, patients with stroke and transient ischemic attacks should be investigated for these conditions."

LESSONS IN GERIATRIC MEDICINE

The care of elderly patients is far more complex than treatment of younger people, yet clinicians too often ignore this difference. The medical school has received a $2 million grant from the Donald W. Reynolds Foundation to teach medical students how to care for the aging population. "With the elderly, any problem has many causes and consequences that need to be understood," said Margaret A. Drickamer, M.D., associate professor of internal medicine and geriatrics at Yale, and lead investigator on the project. "It means asking more questions and asking different questions." Drickamer hopes to integrate geriatric medicine into existing curricula. "We don't want to take away from existing programs," she said. "We just want to make sure the concepts are taught."

JOHN CURTIS

In their first collaboration, Nina and John Rose mixed a common livestock virus with HIV proteins to produce a vaccine that has kept infected monkeys AIDS free.

AIDS VACCINE CLEARS FIRST HURDLE

Livestock virus is the vector for agent that works in monkeys; nasal administration seen as plus.

A vaccine that uses an attenuated livestock virus as a vector for two *hiv* proteins has kept infected monkeys free of *aids* for more than a year, according to a team led by Yale scientists. The vaccinated monkeys, some infected with a highly pathogenic simian *aids* virus for as long as 14 months, have not developed full-blown *aids* and their viral loads have remained low. The vaccine shows promise in another area; it can be administered through nasal drops rather than by injection, making it more affordable and practical for use in developing countries, where *aids* is taking its heaviest toll.

"Based on our results we think it is likely that this vaccine could be an effective *aids* vaccine in humans," said John K. Rose, *ph.d.*, professor of pathology and of cell biology. Rose and his wife, Nina F. Rose, *ph.d.*, an associate research scientist, led a team that included scientists at Yale, the Aaron Diamond *aids* Research Center, Tulane University, Duke University and the Gladstone Institute of Virology and Immunology. Their results were published in the September 7 issue of *Cell* and presented at the *aids* Vaccine 2001 Conference in Philadelphia in September.

The virus, vesicular stomatitis virus (*vsv*), is a preferred vector for vaccines because it provokes a strong immune response. Although never tested in humans, *vsv* has proved effective in animal models as a vector for influenza and measles vaccines. The combination of the virus and two *hiv* proteins called Env and Gag put the monkeys' immune systems on high alert, making them more effective against *hiv*, John Rose said.

"It is a very strong stimulator in both arms of the immune system—the antibodies and the cellular immune system," he said. "This holds down the spread of the infection in the animals. There are fewer infected cells. It is less of a task for the immune system to hold the virus in check and the viral loads go down to very low or below detection."

The ability to deliver the vaccine in drops rather than through needles, said Rose, is crucial in developing countries. "It would be impractical and very expensive to inject millions of people with *dna* vaccines," he said. "The *vsv*-based vaccine would be a cost-effective and equally successful alternative to other vaccines that have been tested." In addition, the vaccine proved far more effective when administered nasally than when injected intramuscularly.

In two studies carried out over the past four years, the team vaccinated seven monkeys and left eight monkeys in a control group with no vaccination. All 15 monkeys were then infected with a hybrid of human and simian *aids* viruses. "We found that seven out of the eight unvaccinated monkeys developed *aids* in an average of five months, while vaccinated monkeys have been *aids* free for up to 14 months," Rose said.

Wyeth Lederle Products Corp. has licensed rights to the vector and is conducting further animal tests in collaboration with Yale scientists before proceeding to clinical trials.

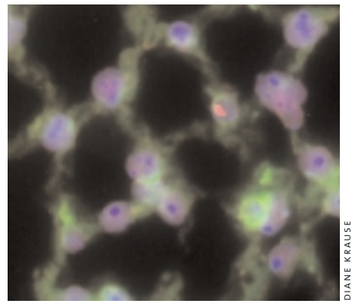
IN A STUDY IN MICE, ADULT STEM CELLS REVEAL THEIR VERSATILITY

Stem cells derived from the bone marrow of adult mice, a Yale researcher and her colleagues have found, can create not only new bone marrow cells, but liver, lung, gastrointestinal and skin cells. "Thus far, this is the closest adult-derived stem cell to the embryonic stem cell, which can transform into any cell type in the body," said Diane Krause, *m.d.*, *ph.d.*, associate professor of laboratory medicine and pathology. Krause was lead author of the study, which was carried out by scientists from three institutions. Their study was published in the journal *Cell* in May.

The research built on the same group's earlier experiments in mouse models that showed that bone marrow cells could generate new liver cells, including hepatocytes and cholangiocytes (*Findings*, Fall 2000 | Winter 2001). Krause and her colleagues then showed that this regeneration also occurs in humans. "However, we didn't know if the bone marrow cell that could make liver was the same cell that could make blood," Krause said. "We wanted to know what cell it was."

In their most recent experiment, Krause and her collaborators irradiated female mice, then transplanted a single male-derived cell. Using the Y chromosome as a marker, they identified the progeny of that cell. To their surprise, they found the male chromosome not only in the blood and bone marrow, as expected, but also in 15 di=erent cell types. "The adult bone marrow cell, we have found," said Krause, "has remarkable plasticity."

The other principal investigator on the project was Neil Theise, *m.d.*, associate professor at New York University School of Medicine. Saul Sharkis, *ph.d.*, of the Oncology Center at Johns Hopkins School of Medicine, was the senior author. Other collaborators were from the Department of Genetics at Yale and the Department of Pathology at the *nyu* School of Medicine.



DIANE KRAUSE

After a female mouse received bone marrow from a male mouse, the transplanted stem cells generated up to 15 different tissue types, including lung tissue (above). A team led by Diane Krause used the male's Y chromosomes, shown in pink, as markers.

et cetera

NEW GENES FOR HYPERTENSION

A team of Yale scientists has identified mutations in two genes that cause a rare form of hypertension. The finding has also uncovered a previously unknown metabolic pathway governing blood pressure that could offer new targets for medications.

The finding, reported in the August 10 issue of *Science*, identifies genes on chromosomes 12 and 17. In their mutated form they can cause increased reabsorption of salt by the kidneys and impaired secretion of potassium and hydrogen ions. This leads to a rare form of hypertension called pseudohypoaldosteronism type II.

The principal investigator on the study was Richard P. Lifton, M.D., PH.D., professor of genetics, medicine, and molecular biophysics and biochemistry and an investigator for the Howard Hughes Medical Institute.

AN HERBAL CLUE TO INFLAMMATION

An herb commonly used to treat migraines inhibits a protein that causes inflammation, Yale pharmacologists have found. In an article published in the August issue of *Chemistry & Biology*, a team led by Craig Crews, PH.D., associate professor of chemistry, pharmacology, and molecular, cellular and developmental biology, showed that a component of the herb feverfew targets a protein called IkappaB Kinase, which is responsible for inflammation. "Now that we have identified an inhibitor of this protein," said Crews, "that information can be used to develop additional inhibitors."

A CASE OF HIDE AND SEEK?

Treated early, Lyme disease is usually cured with antibiotics, but the prolonged form of the disease can be more troublesome. Yale scientists have observed that while the Lyme spirochete is easily digested by immune cells *in vitro*, rare bacteria within the body can withstand the onslaught of the immune system, perhaps explaining the spirochete's ability to survive long-term. Ruth R. Montgomery, PH.D., set out with colleague Stephen Malawista, M.D., to determine whether the spirochete somehow weakened the immune system. Results of a study of mice published last June in the *Journal of Infectious Diseases* strongly suggested that this was not the case. With defects in leukocyte function all but ruled out, the team will look next at the other side of the equation: how the spirochete may be masking itself from immune surveillance.

Health Networks: Can They Be the Solution?

by Thomas P. Weil, *ph.d.*, *m.p.h.* '58

The University of Michigan Press (Ann Arbor, Mich.), 2001

This book evaluates whether recently formed health networks can generate enough fiscal savings to provide greater access to and quality of health care despite the current trend of cutbacks in reimbursement from Medicare and managed-care plans. It concludes with a very timely and much needed discussion of how U.S. health networks might divest certain programs, services and facilities in the case of an almost inevitable economic turndown.

Quantitative Evaluation of HIV Prevention Programs

edited by Edward H. Kaplan, *ph.d.*, the William N. and Marie A. Beach Professor of Management Sciences and professor of public health, and Ron Brookmeyer

Yale University Press (New Haven), 2002

How successful are HIV prevention programs? Which HIV prevention programs are most cost effective? Which programs are worth expanding and which should be abandoned altogether? This book addresses the quantitative evaluation of HIV prevention programs, assessing for the first time several different quantitative methods of evaluation.

How to Have Magnificent Sex: The 7 Dimensions of a Vital Sexual Connection

by Lana L. Holstein, *m.d.* '75

Crown Publishers (New York), 2001

Holstein has been helping men and women find their vital sexual connection for 25 years. By experimenting with all dimensions—understanding the body, exploring the senses, recharging desire, opening the heart, boosting intimacy, baring the soul and embracing the spirit—Holstein says couples can achieve a more perfect union.

Adolescent Medicine: Adolescent Cardiology

edited by Christine A. Walsh, *m.d.* '73, and Robin W. Doroshow, *m.d.*

Hanley & Belfus, Inc. (Philadelphia), 2001

The purpose of this volume from the *Adolescent Medicine: State of the Art Reviews* series is to discuss practical and important topics concerning heart disease—both suspected and confirmed—in the adolescent.

Skeletal Injury in the Child, 3rd Edition

by John A. Ogden, *m.d.* '68

Springer-Verlag (NewYork), 2000

For clinicians and residents, this comprehensive text includes new chapters covering the subjects of polytrauma, growth plate disorders and their treatment, the pediatric athlete and an overview of nonoperative and operative approaches to children's fracture care.

The Stranger in the Mirror: Dissociation—The Hidden Epidemic

by Marlene Steinberg, *m.d.*, former research a ; liate in psychiatry, and Maxine Schnall

Cliff Street Books (New York), 2000

Based on Steinberg's 18 years of research, this book debunks the myths associated with dissociative disorder, presents her own revolutionary test which allows readers to assess the severity of their own problems and introduces the innovative therapy known as the "Four C's" to cure dissociation.

The Yale Management Guide for Physicians

by Stephen Rimar, *m.d.*, *hs* '87, *m.b.a.*

John Wiley & Sons (New York), 2001

From health care policy and health economics to health care marketing and negotiating, this comprehensive guide addresses all of the major issues affecting the delivery of health care services in the 21st century. This manual helps doctors acquire skills they need to expand their practices; to develop, articulate, and advocate ideas; discuss and manage the decision-making process and assume a leadership role in the health care industry.

Alternative Medicine and Multiple Sclerosis

by Allen C. Bowling, *m.d.* '88, *ph.d.*

Demos Medical Publishing (New York), 2001

In a handy, practical format, this book offers reliable information on the relevance, safety and effectiveness of various complementary and alternative therapies that are not typically considered in discussions of MS management but are in widespread use.

Parenthood Lost: Healing the Pain after Miscarriage, Stillbirth, and Infant Death

written and edited by Michael R. Berman, *m.d.*, *hs* '76, clinical professor of obstetrics and gynecology

Bergin & Garvey (Westport, Conn.), 2001

Berman is the creator of Hygeia (www.hygeia.org), an online community for bereaved parents who have lost a pregnancy or newborn child. Here he shares insights from his experiences helping parents deal with their grief and unravels the confusing genetic and medical causes of miscarriage, stillbirth and infant death. Through original poetry, firsthand stories told by parents and articles describing genetic and medical disorders, this book offers clarification and hope for parents who have suffered this tragedy.

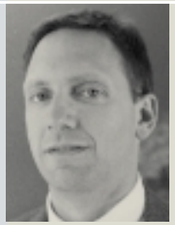
The descriptions above are taken from the book jackets.

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.

JOYCELYN ELDERS

A hub for health care

Schools can provide access to health care for children who might not otherwise see a doctor, former U.S. Surgeon General Joycelyn Elders, M.D., said during a visit to New Haven in early July. Speaking to teachers, principals, program directors and policymakers at the 12th annual conference of the School of the 21st Century (21C) initiative, Elders urged schools to establish clinics focusing on prevention. "You can't educate people who are not healthy, and you certainly can't keep people healthy if they're not educated," said Elders. Established in 1988, the 21C initiative was founded by Edward F. Zigler, PH.D., one of the principal architects of the federal Head Start Program, Sterling Professor of Psychology and a faculty member in the Child Study Center. More than 1,300 schools in 20 states have adopted the program, which transforms schools into multiservice centers providing a variety of resources for children, parents, teachers and child-care providers.



ALAN S. RUDOLPH

Guarding against germ warfare

When federal officials simulated a bioterrorist attack on Denver, Colo., last year, "the city was lost," said Alan S. Rudolph, PH.D., M.B.A., a program manager at the Defense Advanced Research Projects Agency. "They had to close the borders of the state of Colorado and they still couldn't contain the pathogen they were modeling, a strain of plague."

In remarks that seem prescient today after the terror attacks on the East Coast, Rudolph discussed the Colorado simulation exercise during a talk at surgical grand rounds in May. His topic? "Technological Challenges in Defending the U.S. against Biological and Chemical Warfare." The simulation, Rudolph said, "taught us that we are ill-prepared to deal with this problem." The military, he continued, must rethink its traditional mission of defending against a nuclear threat from a large adversary. "It is clear that a small number of people can perpetrate a fairly large effect," he said. Protection efforts require the coordination of different agencies, he said. On September 20, President Bush announced a new cabinet position for homeland security to unify the government's anti-terror efforts.

DAVID R. WILLIAMS

Racial disparities and community health

"The driving force behind racial inequality in health," said David R. Williams, PH.D., "is the economic circumstances of social groups." Williams, a sociology professor at the University of Michigan and former Yale faculty member, was a keynote speaker in May at a conference titled "The Impact of Poverty on Individual and Community Health," sponsored by the Department of Psychiatry's Division for Prevention and Community Research. "Economic status is accounting for most of the racial difference in health, but not all of it," Williams said. "Poor white men still live longer than poor black men. The racial differences in economic status are not an act of God, but reflect the implementation of racial policies in society that have predictable outcomes."

RACHEL NAOMI REMEN

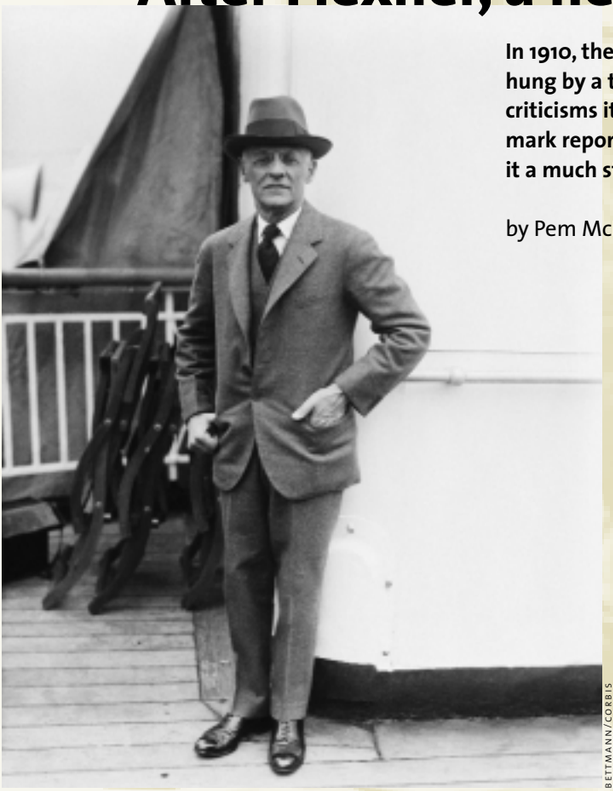
Healing outside the box

When Rachel Naomi Remen, M.D., spoke about the will to live at the Yale Cancer Center in May, she touched more than once on medicine's preoccupation with control. "We may be so deeply into the pursuit of mastery," said the author of the national bestseller *Kitchen Table Wisdom*, "that we may not see mystery when it happens directly in front of us." Remen told of a patient she treated as an intern at Memorial Sloan-Kettering whose bones and lungs were riddled with cancer. During a two-week hospitalization, his lesions disappeared for no apparent reason. "Were we in awe?" said Remen. "Certainly not. We were frustrated. It was obvious we had misdiagnosed this man." Pathologists consulted for a second opinion concurred with the original diagnosis of osteogenic sarcoma. When the patient was presented at grand rounds, the 250 physicians there concluded that the chemotherapy that had been stopped 11 months before had suddenly worked. "I sometimes wonder if too great a scientific objectivity can actually make you blind," said Remen. "It was 15 years before I began to question this conclusion. When everyone is thinking inside of the box, it is hard to think anything new, but outside the box is often where life is."

After Flexner, a new start

In 1910, the medical school's fate hung by a thread. The deep criticisms it weathered in a landmark report ultimately made it a much stronger institution.

by Pem McNerney



BETTMANN/CORBIS

The Flexner Report of 1910 prompted Yale and many other medical schools in the United States to make fundamental changes. Author Abraham Flexner, above, recommended that Yale School of Medicine remain open but that it bolster its fund-raising and hire full-time faculty, among other improvements.

The release of the Flexner Report in 1910 was bad news for most of the nation's medical schools. Commissioned by the Carnegie Foundation for the Advancement of Teaching to evaluate the ability of U.S. medical schools to train new doctors, consultant Abraham Flexner's verdict was that most weren't up to the task. He recommended that the vast majority of schools be shut down; in New England, he said, the only two worth saving were Yale and Harvard. And despite the tacit endorsement, the report singled out Yale's thinly stretched faculty as a weak point. "The instructors ... are overworked, being called on to carry the routine work of extensive subjects in all their parts without adequate assistance. Under such circumstances, the work, however conscientious, is bound to be limited." The report also recommended that the school obtain a larger permanent endowment.

The School of Medicine's bleak condition at the turn of the century and its successful e=orts to rehabilitate itself are the subject of *Medicine at Yale, 1901–1951*, the second in a series of exhibits at the Cushing/Whitney Medical Library marking the University's Tercentennial this year. The exhibit, which has been adapted for the web, shows how, in the 1920s, the school transformed itself from a mediocre institution with part-time faculty and limited resources into one of the nation's top medical schools. With a full-time sta=, new facilities and many new departments, including the innovative and controversial Institute of Human Relations, the school generated enough momentum in the '20s to survive both the Depression and World War II intact.

The Flexner Report's grim assessment of Yale's resources and facilities came as no great surprise to the school, which had been struggling for its survival since the 1880s. Herbert E. Smith, dean from 1885 to 1910, had made some improvements. He tightened entrance requirements, expanded the curriculum and made e=orts to establish closer ties with New Haven Hospital. His successor, George Blumer, dean from 1910 to 1920, was able to establish a sorely needed, more functional system for key faculty, providing them with a full-time salary for teaching and research. He also oversaw the growth of the endowment fund and forged an agreement with New Haven Hospital that allowed the school to take charge of the wards and use them for medical education. One of Blumer's proudest achievements was the establishment of the Department of Public Health in 1915, with Charles-Edward Amory Winslow as its founding chair.

In 1920, Milton C. Winternitz became dean. He oversaw the construction of the Sterling Hall of Medicine, the expansion of clinical facilities and the establishment of several departments, including the Department of Pediatrics (1921), the Department of Obstetrics and Gynecology (1921) and the Psychiatry Group (1935). During his tenure, the Department of Surgery was moved to a full-time basis and the Yale System of Medical Education was established. Under the Yale System, medical students were treated like graduate students, required course exams were eliminated and electives were encouraged. The Institute of Human Relations, specializing in interdisciplinary research in medicine, law and the social sciences, was created in 1931. According to the exhibit text, "Winternitz evoked strong emotions in his colleagues. To some he was brilliant, bold, and a 'steam engine in pants,' and to others he was an insu=erable 'martinet,' a Napoleon, and an anti-Semite" though he was Jewish himself. In 1935 he was forced to step down from his post as dean, continuing on as chair of pathology until his retirement in 1950.

Yale had three more deans during the first half of the century: Stanhope Bayne-Jones (1935–1940), Francis Gilman Blake (1941–1947) and Cyril Norman Hugh Long (1947–1952). Among other notable accomplishments, they succeeded in getting the medical school on solid financial ground so that it could continue to grow following World War II.

HISTORICAL LIBRARY OF THE CUSHING/WHITNEY MEDICAL LIBRARY (5)

More on the Web
info.med.yale.edu/ymm

To view the online exhibit *Medicine at Yale, 1901–1951*, please visit our website and select EXTRAS.

FROM TOP

George Blumer, dean of the medical school from 1910 to 1920, started making many of the reforms that were needed to improve the school's operations. When Blumer stepped down as dean in 1920, he became the David Paige Smith Clinical Professor of Medicine until he retired in 1940.

Harvey Cushing was enormously fond of Yale College, his alma mater. But when the University invited him to become a professor of surgery in 1907, he declined the offer because he felt Yale did not have adequate control of clinical facilities at New Haven Hospital. He went on to have a distinguished career as a neurosurgeon at Johns Hopkins and Harvard. Then, upon his retirement from Harvard, he came to Yale as a professor of neurology in 1932. His rare book collection was bequeathed to Yale in 1939.

Milton Winternitz, dean from 1920 to 1935, presided over the boom years of the medical school following World War I, when it emerged as one of the top medical schools in the country. Winternitz embarked on a campaign of building buildings, hiring faculty, organizing departments and raising money to finance it all. The son of an immigrant doctor, Winternitz was controversial and evoked strong feelings among his colleagues. He was forced to step down as dean in 1935, but continued on as chair of pathology until his retirement in 1950.

In 1916, the Yale School of Medicine admitted women students for the first time. Louise Farnam was one of two women to graduate in 1920. She won the Campbell Gold Medal for scholastic achievement. Her classmate, Helen May Scoville, was later hired by Yale as an instructor.

BACKGROUND During World War I, the medical school organized a mobile hospital unit. It arrived in France in early 1918, spent the winter in Limoges and moved to the front during a major German offensive. The group improved its efficiency to the point where it could operate on one badly wounded patient every 45 minutes.

Sharks, salt

(and a taste of lobster)

An intensive week at the bench in Maine introduces students to modern lab strategies and techniques, ancient DNA and a clambake to write home about.

Text and photographs by John Curtis

A slice of a shark's rectal gland captures the attention of Jenny Blair, Vicash Dindwall and Dena Springer as Ignacio Gimenez, a postdoctoral fellow in physiology, guides them through an experiment at the Mt. Desert Island Biological Laboratory in June. The Yale students isolated a protein in the gland, then measured its response to phosphorylation.

Few medical students can say that, as part of their education, they plucked a writhing dogfish shark from a pool of water. Or that they ended their first year by seeking clues to human disease in the organs of a fish that reached its evolutionary peak more than 300 million years ago.

This past June that pool of sharks lured about two dozen Yale students to Salisbury Cove, Maine, just a few miles from Bar Harbor. For more than a century, scientists at the Mt. Desert Island Biological Laboratory here have explored the genes shared by fish and humans. For about half its lifetime, the laboratory has had strong ties to the School of Medicine, a relationship that began in the 1950s, when Franklin Epstein, *m.d.* '47, *hs* '49, professor of medicine, began bringing residents and fellows to Maine. In June 2000, for the first time, medical students arrived for a week's training in bench research. This year another group of students repeated the Intensive Pedagogical Experience, a program designed to introduce them to the strategies and techniques of laboratory science and to encourage them in careers as physician-scientists. Most of the students arriving in June had just completed their first year of medical school; the group also included a student who began med school this fall.

In the course of their week on Mt. Desert Island, the students cloned genes, learned to synthesize *dna* by means of polymerase chain reaction and generated copies of proteins by inserting *rna* into frog eggs. They also learned the difference between Western blots, used to find specific proteins, and Southern and Northern blots, used to find the *rna* and *dna* for specific genes.

Rupali Gandhi, who is beginning her second year at Yale this fall, majored in biology as an undergraduate, then went on to get a law degree at Yale before taking up medicine. "I hope to come away from this course with a better understanding of a lot of research methods so that the next time I read a journal article my eyes won't glaze over the methods section," she said, sitting on a porch outside one of the many laboratory buildings scattered throughout the forest. Understanding research strategies and gaining familiarity with the scientific method are among the goals of the course, according to its director.

"The idea of rigorous pursuit of a question and a clear hypothesis is applicable to all that students do in research at Yale," said John N. Forrest, *m.d.*, *hs* '67, who heads the Office of Student Research at the medical school and is director of the Mt. Desert Island Biological Laboratory, where he has spent the last 32 summers.

Long before the first group of Yale students traveled to Maine, the notion of an intensive laboratory experience was brewing in the mind of Dean David A. Kessler, *m.d.* As an undergraduate at Amherst College, he spent four weeks one summer at the Woods Hole Marine Biological Laboratory. The time he spent studying macrophage inhibition factors in sea urchins served as a model for the program in Maine. Kessler wanted to provide students with both hands-on laboratory experience and a chance to interact closely with faculty. "You get to see things you just don't see sitting in a lecture hall," he said. "This is what education should be." And holding the course on Mt. Desert Island freed students and faculty from the day-to-day distractions of being on campus.

Nestled amidst hundreds of acres of woodlands, the buildings at the Mt. Desert Island Biological Laboratory belie their true purpose. Although it resembles a rustic fishing camp, the laboratory is the summer home to scientists from around the world.

The view from the laboratory's dock on Mt. Desert Island's northern shore takes in evergreen forests and rocky shores typical of the Maine coast.

Lab assistant Sarah Decker extracts the rectal gland from a spiny dogfish shark just plucked from the laboratory's pool. Local fishermen provide a steady supply of the spiny dogfish, the only shark species found in these waters.

Forrest scheduled the course for early June, after students have completed their medical school course work and before the lab's high season in July and August, when its year-round population of 17 staff members swells to more than 200 principal investigators, postdocs, graduate students and laboratory technicians.

Amidst the laboratory's 350 acres of poplar, pine, spruce and cedar forest, the hierarchy that typically rules academia takes a sabbatical. First of all, the laboratory, with its shingled and weathered buildings in the woods, looks more like a fishing camp than a research center for top scientists from more than 50 institutions. But enter those buildings and you'll see they're filled not with lobster pots and fishnets, but with beakers, pipettes, computers, centrifuges and a gene sequencer. Dress is informal. As often as not, students and faculty wear T-shirts, shorts and sandals. They spend most of their waking hours together. And, most troubling for some students, only first names are used. "We all know him as Dr. Forrest because he's the head of research," said student Dena Springer. "We come here and he's John."

At the heart of the students' experiments is the rectal gland, an organ unique to sharks and other fish. Local fishermen provide a regular supply of spiny dogfish sharks, also known as *Squalus acanthias*, a relatively benign member of the shark order. Between 16 and 20 inches long, they are decidedly passive compared to their great-white cousins. Students say these fish will bite, but only if you stick a finger in their mouths. Their rectal gland is a highly specialized organ whose only function is to pump salt. Among the gland's virtues is its relatively large size, about an inch long, making it easier to manipulate for neophyte researchers than cells or molecules.

Examining a fish's ability to control its salt may seem a highly esoteric field of study. Yet the rectal gland offers clues to understanding cystic fibrosis, the most common fatal childhood disease and one that is also concerned with salt imbalance. It is caused by a genetic disorder, the malfunction of a protein called the *cftr* chloride channel, which renders the body unable to regulate chloride transport. Without the proper functioning of this protein, a sticky mucous secretion develops, clogging lungs, sinuses and the digestive system.

Working in four groups of six, the students approach the gland from various perspectives. Over the course of a week they try to answer these and other questions: What is the function of the rectal gland in the shark? How is secretion by the gland regulated by known agents and second messengers? What is the function of *cftr*? Can we determine Na-K-Cl cotransporter activation in an isolated cell preparation? What is the importance of single nucleotide polymorphisms in the post-genome era?

Students may look at the entire organ, measuring its function with agents such as barium, forskolin or *ibmx*, which inhibit or stimulate chloride transport. For another experiment, working with tissue from the gland, they isolate a protein and try to turn on and off its capacity to transport sodium, potassium and chloride. They may phosphorylate the protein and look for signs of activity. When they look through a confocal microscope, the students expect to see a lot of green, a sign that phosphorylation has activated the cotransporter protein. They also take the *cftr* chloride channels they've generated in frog eggs and measure their electrical activity. Continuing that experiment, they add hormones to open and close the channels.

The science behind the experiments was complex, and at times the mechanics could be demanding and repetitive. One rainy afternoon medical student Jenny Blair watched as a shark's salt gland excreted liquid into a narrow-bore pipette several inches long. When the pipette filled, every few minutes or every few seconds, depending on whether chemical agents were involved, she inserted a new pipette into tubing coming from the gland, while others on her team measured the amount of liquid, then determined how much chloride it contained. Upon completing the experiment, they calculated the gland's ability to excrete chloride under the conditions studied.

Part of the students' fascination comes from knowing that another team in another lab or rotation will pick up on their experiments. "We took the body parts of a shark and extracted *rna* from them," said student Benjamin Negin, describing a typical research sequence. "Then we passed the baton on to the next group. They're turning the *rna* into *dna*. The final group is using polymerase chain reaction of the *dna* to identify what it is."

Niya Jones and Bao Duong were part of the second team in the sequence Negin described. They learned how to manipulate a pipette to insert shark *dna* into an agarose gel. They were filtering the *dna* by size, looking for the genes related to a family of proteins that regulate chloride transport. Steve Aller, a doctoral candidate at Yale, guided them through the process, teaching them how to hold the pipette so the *dna* slips into a well in the gel without smearing.

When, at the end of their experiment, they found a set of small genes they could not identify, Jones and Duong passed them off for further research to the next team in the rotation. "If it's a subunit of the *cftr* channel or an unrelated protein, it would be

TOP At the bench in his lab, John Forrest instructs a group of students in the experiment they will undertake, which involves manipulations of the rectal gland's ability to excrete salt.

BOTTOM Steve Aller, a doctoral candidate at Yale, instructs medical student Niya Jones in the use of a pipette for an experiment with shark DNA.

The week in Maine ends with a clambake, campfire and sing-along at a park on the island's "quiet side."

interesting to see," said Spencer Epps, who planned to compare the genes to those in an online database at the National Institutes of Health.

Not all the experiments yield clear results. In presenting their findings students were refreshingly honest about the successes and failures of their experiments, as well as the unanswered questions. "We don't have wild-type data," said one student whose team explored mutations in ion channels, "because it got messed up." "The sequencing did not work," said a member of Epps's group, which had hoped to identify unknown genes, "and we're not sure why." Most experiments proved successful, insofar as the students noted patterns of behavior in the way cells responded to stimulants and inhibitors. For example, John Koethe explained the slopes and valleys on a graph that tracked the rectal gland's response to different agents. "They show barium inhibition, recovery, then inhibition," he said. Another group working with rectal gland slices and tubules found that forskolin and *ibmx* activated the chloride channel, leading to chloride excretion. Working with the whole gland, one team reported inconclusive results of their experiment; a high dose of potassium inhibited chloride secretion but a low dose yielded mixed results that offered no firm conclusions as to its effect.

The experiments conducted here are a natural outgrowth of the laboratory's focus on the physiology of marine and human organisms. Sharks, for example, reached evolutionary perfection between 300 million and 400 million years ago and have changed little since. Their genome is about 70 percent identical to that of humans. "Humans adopted many of the successful systems they evolved," said James L. Boyer, *m.d.*, *hs* '67, Ensign Professor of Medicine and director of the Yale Liver Center, who heads the Mt. Desert Island Biological Laboratory's board. "That is why we are able to use those marine creatures for relevant research on human systems. The differences are far fewer than the similarities."

Since its founding as a summer school for Tufts University students in 1898 in South Harpswell, Maine, the biological laboratory's focus has shifted between education and research. It first taught marine biology to undergraduates, but quickly became a center for marine research as well. In 1921 a land-holding organization, Wild Gardens of Acadia, offered the lab 100 acres on Mt. Desert Island. George B. Dorr, one of Wild Garden's leaders, was instrumental in founding Acadia National Park and had a vision for Mt. Desert Island. "He believed this pristine setting would be an ideal circumstance for the study of nature," said Jerilyn Bowers, director of development and public affairs at Mt. Desert Island Biological Laboratory. "He wanted this to be a very cultural, artistic society."

The laboratory was founded at a time when scientists had embraced Darwinian thought and looked for answers to human biology in the sea, where life began. Dozens of marine biology labs sprang up, but only three in New England have lasted: Woods Hole, Cold Spring Harbor Laboratory in New York and the Mt. Desert Island Biological Laboratory. Of the three, only the Mt. Desert Island laboratory continues to study links between fish and humans. Among its neighbors on Mt. Desert Island is The Jackson Laboratory, the world's largest mammalian genetic research facility, which specializes in breeding genetically engineered mice for research. As a research center the Mt. Desert Island Biological Laboratory has brought forth significant discoveries, said Bowers. "Much of what we know today about how the kidney functions came from early research conducted here," she said. The c*dna* of several sodium chloride transporters was first cloned here by two scientists now at Yale, Steven C. Hebert, *m.d.*, chair of the Department of Cellular and Molecular Physiology, and Biff Forbush, *ph.d.*, professor of cellular and molecular physiology.

A quarter-century ago the laboratory renewed its educational focus by offering programs for both graduate and high school students, along with conferences and symposia for scientists from around the world. Still going strong is an eight- to 10-week summer science program for high school students from surrounding Hancock County. (One of those alumni, Aller, is now a *ph.d.* candidate in molecular biophysics and biochemistry at Yale and an instructor in the summer program for Yale medical students.) It is also strengthening its research component with a five-year plan to recruit three scientists who will be the laboratory's first year-round researchers.

Throughout the years, according to those who know it well, the lab worked its magic through an informal environment that brought together biologists, physicians, basic scientists and students and, by its remoteness, encouraged cross-fertilization of ideas. "It is more conducive to learning and picking up different approaches than if you just stay with your own groups," said Boyer. "At Yale," he added, "you have to go out of your way to make those interactions. Here, you can't help but do that."

For medical students, it is these interactions that make the experience worthwhile. In their evaluations of the program's first year, students said that the opportunity to work in small groups with faculty was one of its most attractive features.

More on the Web
info.med.yale.edu/ymm

To explore the Mt. Desert Island Marine Biological Laboratory online, please visit our website and select EXTRAS.

Rupali Gandhi, the student now starting her second year of medical school, agreed. "You can ask as many questions as you want as many times as you want," she said, "and get very clear explanations."

Joining Forrest on the faculty this year were Forbush and Raymond Frizzell, *ph.d.*, chair of the Department of Cell Biology and Physiology at the University of Pittsburgh. (Frizzell arranged a similar program this year for medical students from Pittsburgh, who arrived a week before the Yale students.)

If the first year of the Intensive Pedagogical Experience offered any lessons, it was that the schedule left students little time to enjoy Mt. Desert Island. This year, students had a free afternoon and evening every other day. During those free hours Forrest and Forbush led bicycle and hiking tours of the island.

On Friday, the last day of the course, students made their final presentations after lunch and had the rest of the day to themselves. That evening Forrest organized a clambake at Seawall, a picnic area and campground at Acadia National Park in a section of the island the locals call the "quiet side." Forrest arrived early to stoke a bonfire for cooking. Before long, lobsters and bags of vegetables and mussels were steaming in huge pots of seawater as the sun set over the rocky shore.

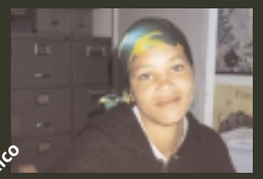
Earlier in the week Forrest sat on a wooden chair outside his lab on a bluff overlooking Mt. Desert Island's Eastern Bay and mused about the course. One of its virtues, he said, is a "conference room" like this, in the shade of a tree with the ocean below. "It's asking a lot," he said, "to say you're going to change people's lives in a week, that people are to change their career goals based on a week's experience. But this course has the potential to encourage people who otherwise might not think about a research career. Some of these students have never run a gel, ground up tissue or looked at cells under a microscope in a research mode before. Here we have very bright students learning all this medicine from lectures, books, videos and the Internet. Unless they are looking inside a cell, thinking about how to study some component of how that cell functions, unless they are striving to interpret what really exists, from their own questions, they are going to be passive recipients. The idea of hands-on work is often so illuminating that it leads people to say, 'This is what I want to do for the rest of my life.'" YM

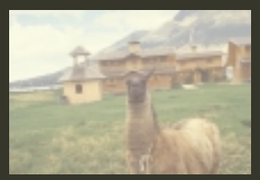
JOHN CURTIS is the associate editor of *Yale Medicine.*

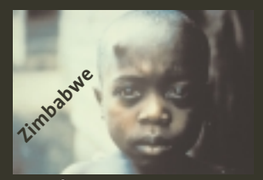
A world OF DIFFERENCE

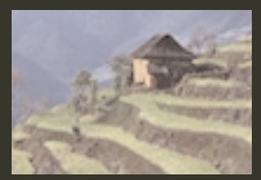
Yale's International Health Program sends young doctors around the globe to provide needed care—and learn the basics of a simpler medicine.

BY CATHY SHUFRO









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IMAGES COURTESY MICHELE BARRY, FRANK BIA, JOEL GALLANT, DELIA RADOVICH AND PHOTODISC

Ramona Farid, *m.d.*, knew she wasn't in New Haven anymore the night she found herself on a hospital patio pouring a patient's urine on an anthill. She was testing for glucose.

If she'd been at Yale, Farid wouldn't have had to think twice about how to follow the progress of a 16-year-old girl in diabetic ketoacidosis, or *dka*; she would simply have ordered finger sticks at two-hour intervals and checked the patient's blood for glucose using a glucose monitor. But this was rural Haiti, where the second-year resident was working for a month with Yale's International Health Program (*ihp*). It was 2 a.m., and there wasn't a test strip to be found at Hôpital Albert Schweitzer.

"I said, 'How the heck am I supposed to manage *dka* without Chemstrips?'" recalled Farid.

Finding low-tech (or no-tech) strategies for diagnosing and treating patients is one of the challenges for residents like Farid who take part in the Yale *ihp*. Since 1981, the popular program has sent residents in internal and emergency medicine to serve more than 300 rotations overseas or in Indian Health Service hospitals in the United States. This year, 40 of the 100 residents in internal medicine will spend four to eight weeks in locales ranging from Alaska to Zimbabwe. They will be the first to be sponsored by a grant from Johnson & Johnson that will fund the 20-year-old program and allow it to expand.

That night in Haiti, Farid realized she understood enough about diabetes to monitor her patient's ketoacidosis without Chemstrips. Talking on the phone with the Haitian attending, she saw the logic behind the anthill approach. In a patient in *dka*, glucose levels would be high not only in blood, but also in urine. By observing how many ants were attracted by the sugar in the girl's urine compared to urine from someone without diabetes, Farid could track the decline in the patient's glucose levels. And so, for the rest of the night, she went out to the anthill with urine samples every two hours. At 8 a.m., the ants stopped coming. Farid took the girl o= the insulin drip and sent her home with injectable insulin.

The insight that Farid gained in Haiti—recognizing that she had useful knowledge of a disease independent of expensive technology—is one of the goals of the *ihp*, according to Frank J. Bia, *m.d.*, its co-founder with Michele Barry, *m.d.*, *hs* '77. With the extensive use of diagnostic radiology and laboratory testing, said Bia, young doctors today "often are not allowed to think through a diagnosis. The diagnosis might be handed to them on a silver platter, or an *mri* scan." Overseas, residents "have to go back to actually listening and touching. We feel these are very important skills to bring back to the art of being a doctor."

In a retrospective study of the program, residents reported that by practicing back-to-basics medicine they gained confidence in their ability to do physical examinations and came to value them more. The study by Robert Wood Johnson Clinical Scholar Anu J. Gupta, *m.d.* '94, *hs* '00, was published recently in *The American Journal of Tropical Medicine and Hygiene*.

Residents in the program also have the chance to try procedures they rarely get to practice at home. At the Alaska Native Medical Center in Anchorage, second-year resident Walter Lin, *m.d.*, helped with a bone marrow biopsy and saw internists take on other tasks usually reserved for specialists. In South Africa and in Cuba, resident Delia Radovich, *m.d.*, *hs* '01, found that practicing medicine where care is free and resources are limited was liberating. She did not have to document every move she made, haggle with insurers or track myriad confirmatory tests. Working in a medically underserved area, she said, "makes you a better doctor just by realizing the whole world doesn't work the same way the United States works. It makes you more human. It pulls you out of your daily grind, and it brings you back to the real reason you chose medicine, or should have chosen medicine: taking care of patients."

The physician's obligation to care for patients provides the motive for the International Health Program, said Bia. "It's a professional ethic that guides the program. You have a social contract that extends beyond the walls of the hospital, and which others do not have. You have taken the Hippocratic Oath."

Barry, who is president-elect this year of the American Society of Tropical Medicine and Hygiene, said the goal of the program is "not to train tropical disease doctors but to instill a sense of global responsibility. Our philosophy is opening people's minds to underserved areas around the world, not only overseas but also in New Haven."

Alumni of the program have chosen careers reflecting this vision. Gupta's study found that the 130 Yale residents who went abroad between 1982 and 1996 were more likely than their counterparts to practice in public health settings and more likely to care for indigent patients, immigrants, substance abusers and patients with *hiv*. For instance, among the doctors in the study who now practice in public health settings, 10 had participated in the International Health Program, while two had not. Among those in the study with a substantial number of *hiv*-positive patients (more than 20 percent), 30 had gone abroad, while 13 had not.

Joel E. Gallant, *m.d.*, *m.p.h.*, *hs* '89, fits this profile. Having elected a rotation in Haiti in 1987 and one in Tanzania and Zimbabwe in 1988, he now serves as associate director of the Johns Hopkins *aids* Service. "It was always my goal to be working with underserved populations in developing countries," said Gallant. "However, my training at Yale and at Hopkins showed me that there were underserved populations on our doorstep, and that was especially true with *aids*."

The fact that many participants in the program go on to care for marginalized patients appealed to the contributions committee at Johnson & Johnson, according to Conrad Person, its director of international programs. The New Jersey company's credo calls for community and global responsibility. "This program fit," said Person. "Yale was able to demonstrate that people who participated in this program were more likely to develop compassion in the practices they developed years later. This is an exciting program that expands the perspectives of people who are very likely to be leaders in the world of health care in the years to come."

This year's grant from Johnson & Johnson will send 40 residents to Indian Health Service hospitals in Arizona, New Mexico and Alaska and to 12 countries including Fiji, India, Russia, Israel, Brazil, China and Nepal. Next year, the gift will allow the program to expand to include residents from other medical schools as well as physicians with established practices. Bia estimates that the grant will come to about $350,000 annually, covering expenses formerly paid for by the Department of Medicine and income from a travelers' clinic run by Barry and Bia. Yale-New Haven Hospital will continue to pay residents' salaries while they are away.

For Radovich, now a fellow in hematology/oncology at Memorial Sloan-Kettering Cancer Center, the experience of working abroad was invaluable. "I chose Yale for Yale, not even knowing that this program was in place. But I think people should come to Yale in droves, knowing this is an option."

September 11 hasn't diminished the program's ambitions; if anything, it has set the bar higher, Barry told a group of students attending the poster session for the Downs International Health Student Travel Fellowship Program in October. "There is a whole world out there that is going to need you even more," she said to the students, who had conducted research abroad. "As America becomes more xenophobic, and as more health care workers hunker down and stay in the United States, I just hope you keep your global vision." YM

CATHY SHUFRO is a contributing editor of *Yale Medicine* and a tutor in the Bass Writing Program at Yale.

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JOHN CURTIS (3)

Michele Barry, top, and Frank Bia, middle, established the International Health Program in 1981. Anu Gupta, bottom, found in a retrospective study published last year that alumni of the program are more likely to practice in public health settings and care for indigent patients, immigrants, substance abusers and patients with HIV.

An epidemic in the making

Type 2 diabetes poses alarming health risks as obesity soars and exercise is crowded from modern life. Yale investigators are seeking better ways to prevent and treat the disease and to understand the science of fat.

Story by Randi Hutter Epstein, M.D. '90
Photographs by Gale Zucker

We are seeing obesity running rampant, particularly in young adults. It's a major health problem that has gotten increasingly worse in the past five years.

Robert Sherwin

For older adults, is moderate-intensity exercise sufficient to lower the risk or severity of diabetes? Must one exercise a little bit every day or is one intense training session a week just as good?

Loretta di Pietro

For a nation obsessed with fitness, it's a small wonder that so many Americans manage to keep gaining weight. Despite an ever-growing choice of diet products and weight-loss programs, more and more Americans are losing the struggle against an expanding girth—or not fighting it at all. According to the Centers for Disease Control and Prevention, rates of obesity surged 60 percent during the past decade and, today, one in five Americans is considered obese, or 30 percent above his or her ideal weight.

People who are serious about e=ectively battling obesity have generally turned to fitness instructors or nutritionists. But at Yale, fat is also the stu= of serious science, pursued by nearly 100 epidemiologists, pediatricians, endocrinologists, biologists, nurses, biochemists and psychologists, among others. They are all part of the Yale Diabetes Endocrinology Research Center, led by Robert S. Sherwin, *m.d.*, the C.N.H. Long Professor of Medicine and past president of the American Diabetes Association. Founded in 1993 with a grant from the National Institute of Diabetes and Digestive and Kidney Diseases, the Yale diabetes center provides the infrastructure for an active interdisciplinary team representing 16 departments. Its mission is not to trim the American waistline but to find ways to prevent and treat an often-serious consequence of obesity, type 2 diabetes mellitus.

Type 2 diabetes occurs when beta cells in the pancreas lose their ability to produce enough insulin to compensate for defects in glucose metabolism. Unlike type 1 diabetes, an autoimmune disease that destroys the beta cells and all of the body's insulin-making ability, type 2 diabetes leaves patients capable of producing insulin but unable to use it e=ectively. This can result in kidney and heart disease, stroke, blindness, nerve damage and loss of limbs. In 1997, the American Diabetes Association (*ada*) estimated that 16 million Americans had diabetes. According to Sherwin, the number has increased by at least 6 percent a year since then, largely in tandem with the rise in obesity.

Worse, type 2 diabetes, long thought of as an adults-only illness, is now striking increasing numbers of young people, particularly Native Americans, African-Americans, Asians and Latinos. "We are seeing obesity running rampant, particularly in young adults," says Sherwin. "It's a major health problem that has gotten increasingly worse in the past five years."

The Yale group has focused its e=orts on understanding the biology of type 2 diabetes and on crafting strategies to prevent its occurrence in key groups of patients at risk for the disease. These approaches draw in a diverse group of investigators who are interested in everything from the biochemical pathways of glucose metabolism to the best ways to encourage at-risk children and older adults to exercise and follow a healthy diet.

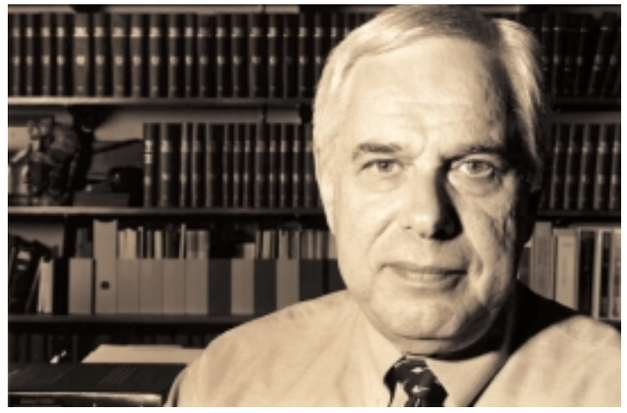
IN VIVO BIOCHEMISTRY

Gerald I. Shulman, *m.d.*, *ph.d.*, has spent the past 15 years exploring the cellular mechanisms of insulin resistance, the defect in the body's ability to use insulin that characterizes type 2 diabetes. Insulin resistance has been shown to be the best predictor for whether or not an individual with a family history of type 2 diabetes will go on to develop diabetes. Recently, his team proposed a new mechanism to explain how an excess of fatty acids in the bloodstream increases the risk of diabetes by interfering with glucose metabolism. "Clearly too much fat is bad for you and somehow it interferes with insulin's ability to stimulate glucose uptake into skeletal muscle. We wanted to know how," says Shulman. To find out, he and collaborators including Douglas L. Rothman, *ph.d.*, Kitt F. Petersen, *m.d.*, Robert G. Shulman, *ph.d.* (no relation to Gerald) and Gary W. Cline, *ph.d.*, have used the tools of nuclear magnetic resonance (*nmr*) spectroscopy to perform what Shulman calls "*in vivo* biochemistry in real time." Their techniques allow researchers to measure metabolic changes noninvasively and with much greater sensitivity than was possible before.

"In the old days, we would have had to perform muscle biopsies to assess the concentration of a metabolite in a particular tissue. Even then we wouldn't have had nearly as clear a picture of what was going on inside the cell because a cell doesn't behave the same once you remove it from the body," says Shulman, the associate director of the Yale Diabetes Endocrinology Research Center, professor of medicine and of cellular and molecular physiology, and a Howard Hughes Medical Institute investigator.

An example of the power of the *nmr* technique was recently demonstrated in a study in which his group used it to measure the amount of fat inside the muscle cells of normal volunteers. They found that higher levels of such intracellular fat are the best indicator of whether or not an individual is insulin resistant.

In order to determine the way in which fatty acids trigger the chemical defects that interfere with insulin's ability to stimulate glucose transport, the Yale researchers infused fatty acids into healthy volunteers and found that they could induce insulin resistance temporarily within five to six hours—demonstrating an inverse link between the presence of fatty acids and the body's ability to metabolize glucose. In subsequent studies the Yale team found that excess fatty acids block insulin's ability to activate phosphoinositol 3-kinase, a key enzyme responsible for mediating



Robert Sherwin

Loretta di Pietro

A tax on fat?

The rise in obesity around the country has led a number of investigators to seek solutions in the realm of public policy. Among those is Kelly D. Brownell, PH.D., director of the Yale Center for Eating and Weight Disorders, who advocates a six-step solution that would, among other measures, impose a tax on foods of poor nutritional quality.

While the idea of a "fat tax" has raised eyebrows (and the ire of many a conservative talk-show host concerned about limits on our right to eat whatever we want), it makes perfect sense to Brownell, a professor of psychology and of epidemiology and public health. He sees a health system far more focused on treatment than on prevention of obesity. He argues that "for every person we successfully treat and remove from the obese population, there are thousands more entering it." In addition to taxing junk foods, his plan calls for publicly financing recreation centers and bike paths, regulating food advertising aimed at children, banning fast foods and soft drinks in schools, subsidizing healthy foods, and incorporating nutrition education in school lunch programs. "I think we have been obsessed with the biology and missed the obvious," says Brownell. "It's the horrible food and lack of physical activity that are causing the problem."

There have never been so many obese children. That is not to say that all these children will become diabetic—because it's not too late.

Sonia Caprio

Clearly too much fat is bad for you and somehow it interferes with insulin's ability to stimulate glucose uptake into skeletal muscle. We wanted to know how.

Gerald Shulman

insulin's capacity to stimulate glucose transport. This is the same step that the Yale scientists, in a study published last year in *The New England Journal of Medicine*, found to be defective in patients with type 2 diabetes. Further research into this pathway could lead to the development of new drugs that are more precisely targeted and carry fewer side e=ects.

In another study, the Shulman group examined whether or not exercise training might be able to reverse the defect in insulin-stimulated glucose transport in the o=spring of patients with type 2 diabetes. In 1995, Shulman's team demonstrated that exercise alone can reduce or reverse this abnormality. In that study, also published in *The New England Journal*, the team examined 10 sedentary adults whose parents had both developed type 2 diabetes and who consequently faced a 40 percent lifetime risk of getting the disease themselves. All of the subjects were insulin resistant but none was obese. The exercise routine consisted of three 15-minute sessions on a stair-climbing machine, four times a week for six weeks. The researchers gave the volunteers glucose intravenously and took blood samples to monitor how well they processed sugar. After one workout, the muscle cells' ability to store glucose improved by 69 percent; after six weeks, by 102 percent. At the end of the study, insulin sensitivity, the ability of the body to use its own insulin, improved by 43 percent. "It's clear that exercise training can reverse the major defect responsible for insulin resistance in these individuals," says Shulman, "and that it is likely to be an e=ective means in preventing or even reversing type 2 diabetes."

AN AGGRESSIVE APPROACH TO TREATMENT

While researchers including Shulman are doing the kind of basic research that leads to new drugs, clinicians are working directly with people vulnerable to the disease, especially children.

"There have never been so many obese children," says Sonia Caprio, *m.d.*, associate professor of pediatrics in the section of endocrinology. She has shown that excess weight clearly carries with it the risk of type 2 diabetes. Last year at the *ada* meeting in San Antonio, Caprio reported that 19 percent of 180 children she tested during the course of treatment for weight disorders had impaired glucose tolerance. "That is not to say that all these children will become diabetic—because it's not too late," she says. "If they do improve their weight and increase exercise, they can prevent it."

Still, a decade ago it was rare for more than 5 percent of all pediatric diabetes cases to manifest themselves in the type 2 form of the disease; most children had type 1 diabetes. Today, in some clinics that number has soared as high as 40 percent, according to Caprio. The phenomenon is so new that epidemiologists haven't yet compiled national statistics by age. To understand what is happening, Caprio began a five-year study last year to determine the metabolic reasons behind the explosion of new cases of type 2 diabetes in children. "We want to learn more about the pathway and where the defect is," she says.

Meanwhile, the race is on to find better ways to treat this new subset of patients before complications set in. Because people with type 2 diabetes usually develop it in middle age, complications often do not arise until their 60s or 70s. For the pediatric patients, the prospect of kidney failure or cardiovascular disease may come decades earlier, in their 30s or 40s.

In August, Caprio was awarded a $3.5 million grant over seven years as the principal investigator at Yale for a multicenter trial to compare standard medical therapies such as insulin and glucophage to newer drugs that have not yet been used in children and adolescents. These include inhaled insulin, insulin sensitizers and insulin secretagogues such as nateglinide. "We propose to be very aggressive in treating the disease in children, rather than taking the usual, laid-back approach," Caprio says. "It used to be the case that you would try to improve diet a little and try a little exercise. But in 10 years, the pancreas is out of shape and the damage is done."

At the other end of the age spectrum are participants in studies conducted by Loretta A. di Pietro, *m.p.h.* '85, *ph.d.* '88, an associate professor of epidemiology and public health and associate fellow at the John B. Pierce Laboratory in New Haven. Working with adults 60 and older, she is studying how fat is deposited and teasing out the di=erences between the physical changes caused by normal aging and those attributable to lack of exercise. Di Pietro is in the midst of a study including dozens of female volunteers at Heritage Village retirement community in Southbury, a 45-minute drive from her o ; ce at Yale. The aim is to study the impact of nine months of exercise training on hormonal regulation and sugar and fat metabolism. Participants agree to provide blood samples and muscle biopsies that will yield information about precisely how exercise seems to reverse or prevent insulin resistance.

The women are divided into three groups. One group does high-intensity aerobic training, jogging on mini-trampolines at about 85 percent of their maximum capacity as measured by heart rate. The second group jogs at moderate intensity. The third group, considered the placebo group, does stretching, tai chi or yoga. The mini-trampolines provide aerobic exercise without

Sonia Caprio

Gerald Shulman

the jarring impact of running on the ground. About five women can work out at a time, which di Pietro says makes the routine more fun and motivates the women to continue exercising when the study is completed.

Fat in the abdominal area, which increases postmenopausally due to the drop in sex hormones, is linked to an increased risk of diabetes, says di Pietro, who is expanding the study to senior centers in New Haven and West Haven. These fat deposits, the deep kind that cover tissues within the abdominal cavity, are much more metabolically active than fat cells in the thighs and buttocks. In addition, there is a decline in both the quantity and quality of muscle mass with aging and disuse.

Researchers theorize that when abdominal fat is broken down, it goes directly to the liver, where it interferes with insulin function and glucose metabolism. Di Pietro and research assistant Jodi Crimmins, *m.s.*, are studying hormonal responses to exercise and, in particular, the e=ect of exercise on growth hormone, insulin-like growth factor and cortisol and how these hormonal changes relate to improvements in whole-body glucose metabolism. The goal is to study how much exercise a subject must perform to garner the anti-diabetes e=ects. Are there gains after one bout of exercise or is long-term training necessary? Is moderate-intensity exercise su ; cient? Must one exercise a little bit every day or is one intense training session a week just as good?

FIGHTING EVOLUTION

As any dieter knows, gaining weight is a breeze compared to losing it. The reason, as is becoming increasingly apparent, has more to do with the evolution of the human species than with gluttony. Humans evolved into a sturdy species because of an inherited ability to prevent starvation, says Sherwin. "We evolved on a planet where food was scarce and you had to work hard to get it. You needed a gene pool to hold onto calories." In other words, those who survived long enough to produce o=spring were able to pass along their calorie-hoarding genes. Those who dropped pounds easily died young. That was good for the survival of the species but is frustrating for those trying to lose weight today.

Recent clues derived from studying the basic biology of the fat cell are lending credence to this theory. Several studies have shown that when individuals reduce their food intake, they also slow metabolism and increase their appetite, thereby negating the impact of fewer calories. Hunger and metabolism are controlled by an intricate system of hormonal signals to and from within the brain. A minor shift in this chemical balance can have a dramatic impact on weight loss or gain.

For instance, a slight change in the hormonal milieu could prompt a craving for, say, an extra hundred calories a day and lead to a gain of 10 pounds in one year. Multiply that by five years, and the average-sized person becomes obese. Sherwin and others at Yale have been studying how leptin, a protein signal released by fat cells, controls appetite. The name for leptin, identified in 1994 by scientists at Rockefeller University, comes from the Greek word *leptos*, which means thin, and its discovery prompted speculation that a better diet pill was on the way. Further research has revealed a much more complex picture, and many questions remain to be answered about leptin and its role in controlling appetite.

Sherwin has shown that leptin acts by binding to receptors in specific regions at the base of the hypothalamus, triggering a cascade of hormonal changes. The leptin cascade, he says, "is a complex system that seems to have an enormous impact on how much we eat.

"Theoretically, if a person has too much fat, the body would stop eating; if there is not enough, the body would increase feeding," says Sherwin. The problem is that individuals who are obese appear to have an altered set point for leptin. "It takes more leptin to shut o= feeding. Then you go on a diet and leptin drops, so you want to eat again." Researchers hope these insights into the leptin receptor will lead to a new approach to weight loss, perhaps a drug that would latch onto the receptor and minimize appetite without slowing metabolism.

As for the genetically blessed—those annoyingly lean people who eat whatever they want without gaining an ounce—scientists have a hunch that they may be endowed with more so-called brown fat than white fat. According to this theory, supported by animal studies, brown fat cells, so named because they have a redder hue due to an increased blood supply, burn calories faster than do white fat cells. The goal, then, for drug-makers would be to somehow increase the proportion of brown cells, promoting fat burning rather than storage.

"We are trying to turn the tables on millions of years of evolution," says Sherwin. "We are not doing too well yet, but at least we are beginning to understand and recognize the problem." YM

RANDI HUTTER EPSTEIN, M.D. '90, has written about medicine for *The Washington Post*, the London bureau of the *Associated Press* and *The New York Times*.

Ronald Duman

Susan Hockfield

Shirleen Roeder

Peter Salovey

Robert Weiss

SENIOR FACULTY HONORED WITH ENDOWED PROFESSORSHIPS

Five faculty members with appointments at the School of Medicine were recently named to endowed chairs.

Ronald S. Duman, *ph.d.*, was appointed the Elizabeth Mears and House Jameson Professor of Psychiatry. He has been on the Yale faculty since 1988, most recently as a professor of psychiatry and pharmacology, and has worked on characterizing the molecular and cellular mechanisms that mediate the long-term e=ects of psychotropic drugs and stress. His research suggests that antidepressant treatments increase the survival and health of neurons and alter their synaptic architecture. Duman's laboratory has also identified several neuropeptide receptors that are expressed in drug reward and craving.

Dean of the Graduate School of Arts and Sciences **Susan Hockfield**, *ph.d.*, was named the William Edward Gilbert Professor of Neurobiology. She joined the faculty in the Section of Neurobiology at the medical school in 1985 and has served as dean of the graduate school since 1998, overseeing the academic and administrative policies of the school, its 2,300 students and 750 faculty. Hockfield has sought to improve the quality of life for graduate students and increase opportunities for informal interaction between faculty and students. Her research work has looked at the molecular substrates involved in brain development, and she discovered a protein in the space around cells that is involved in early development and may play a role in brain tumors.

G. Shirleen Roeder, *ph.d.*, was appointed the Eugene Higgins Professor of Molecular, Cellular and Developmental Biology. Also a professor of genetics, she was part of a Yale team that recently fully characterized the function of the yeast genome. She has studied the process of meiosis by isolating and characterizing yeast mutants defective in the process. She was named a Howard Hughes Medical Institute investigator in 1997. Roeder has been on the Yale faculty since 1981, and her work has appeared in the journals *Cell* and *Science*, among others.

Peter Salovey, *ph.d.*, a professor of epidemiology and public health and chair of the Department of Psychology, was named the Chris Argyris Professor of Psychology. He directs the Health, Emotion and Behavior Laboratory and with John D. Mayer coined the term "emotional intelligence" to describe how people understand, manage and use their feelings. He has focused on how feelings facilitate adaptive cognitive and behavioral functioning. Salovey has also investigated how public health messages can best encourage prevention and early detection behaviors for *hiv/aids* and cancer. He is deputy director of the Yale Center for Interdisciplinary Research on *aids*.

Robert M. Weiss, *m.d.*, was named the Donald Guthrie Professor of Surgery. He is a specialist in pediatric urology and urologic surgery and was listed in the latest edition of "Best Doctors in America: Northeast Region." His research has covered topics from the role of nitric oxide in urinary tract infections and the biochemical and functional changes in the bladders of diabetics to the use of pulse Doppler sonography in the diagnosis of urinary tract obstruction in children. He has been at Yale since 1967 and has served as chief of the Section of Urology since 1988. He also served as interim chair of the Department of Surgery. Weiss received a *merit* Award from the National Institutes of Health for his work on age-dependent factors in ureteral-vesical function and the Urodynamic Society's Lifetime Achievement Award.

AP/WIDE WORLD PHOTOS

The epicenter of the earthquake struck near Bhuj, the capital of Kachchh, and left much of the city in ruins.

HELPING, AND LEARNING, THROUGH DISASTER RELIEF IN INDIA

After an earthquake and as many as 60,000 deaths, Yale students and physicians help shore up health system.

Midway through their 10-day trip to western India in March to help with earthquake-relief e=orts, a team of Yale students and physicians visited the Children's Hospital in Bhuj, a city near the earthquake's epicenter. Shantiben Patel, *m.d.*, the hospital director, had set up tents outside the damaged building and was seeing patients when the team arrived. "She had been working six weeks straight, day and night," said Raj Krishnamurthy, *m.d.*, who practices internal medicine at the VA hospital in West Haven and was a preceptor for the team. "She didn't have a day o=. She was the only pediatrician in the whole area."

Patel quickly put the Yale team to work seeing outpatient visitors while she tended to the neonatal intensive care unit in one of the many tents on the street. Over the next four hours the five students and their two preceptors tended to about 25 children, most su=ering from diarrhea, dehydration, upper respiratory tract infections, malnutrition and urinary tract infections.

The earthquake that struck the western Indian region of Kachchh, on January 26, measured 7.9 on the Richter scale. Estimates of the death toll vary, with the government estimating between 20,000 and 30,000 deaths and relief workers saying as many as 60,000 people may have died. The Yale team, made up of five medical students, a public health student and two physicians, arrived six weeks later to scenes of rubble and ruin. They also found an already fragile health care system in shambles.

In New Haven, students' initial response was a fund-raising drive that netted about $1,000 for earthquake relief. The students wanted to do more and approached Dean David A. Kessler, *m.d.*, who agreed to send six students to India. It was up to the students to organize the trip. Seventeen students applied to go, and six, all but one of Indian heritage, were chosen through an application process. After securing their preceptors—Krishnamurthy and David Litvak, *m.d.*, a third-year resident in internal medicine—and finding a nongovernmental organization to work with, the students were on their way. Upon their return, the students filed a report with the dean's o ; ce.

Kachchh is 17,000 square miles of plains, desert and salt flats bounded on the north by Pakistan and on the south by the Arabian Sea. Most of its inhabitants farm grains, cotton and lentils. Some work in limestone, marble and gypsum mines. In recent years the region has su=ered two droughts and a cyclone. "It's a very di ; cult state to live in as it is," said student Simran Singh.

The team's guide to the region and its medical needs was Anupam Banerjee, *m.d.*, an intern in India fresh out of medical school who had begun a term of service in Kachchh just after the earthquake hit. Banerjee, in turn, was working with the Shrujan Trust, an organization founded in 1969 to provide famine relief. The trust branched out into economic aid by marketing embroideries made by 2,500 craftswomen in 85 villages. It also began medical outreach and provided the van that took Banerjee's mobile medical unit into the countryside to provide primary care.

The students arrived at the Shrujan compound about 20 miles west of the city of Bhuj ready to work, despite a 36-hour trip from New Haven and a 10-and-a-half-hour time di=erence. Their new home was a one-room, thatched-roof hut with a single bed. (Most of the team slept on the floor or outdoors in their sleeping bags.) The next day half the team joined Banerjee on the medical van, while the other half went to the nearby village of Ghada to organize activities for schoolchildren.

Although several members of the group spoke Hindi and one spoke Gujarati, language remained a problem in this country with more than 800 dialects. The dialect spoken in Kachchh was at times incomprehensible to the one Gujarati speaker on the team, Rupal Badani, a third-year medical student. Nevertheless, because of their knowledge of Indian languages and with the help of interpreters, the students managed to communicate.

Within a few days of their arrival, the team undertook a health assessment for Ghada, looking into nutritional patterns and access to health care, prenatal care and primary care. They also organized diabetes and hypertension screenings at a health camp at Shrujan. When it was time to leave, team members felt they had contributed something of value to the relief effort. The presence of the students and physicians on the medical van allowed more patients to be seen. Their survey left health workers a tool for providing medical care to villages. Their diabetes and hypertension screenings were the first for many patients and included follow-up via the mobile unit. And they established a program for children that others would continue after they left.

They also returned to New Haven with valuable experience, having been able to participate in emergency and primary care in a remote setting with limited resources. "We felt like we were doing something for someone, but we were also really learning," said third-year student Vivek Murthy.

JOHN CURTIS

YALE GUJARAT TEAM (2)

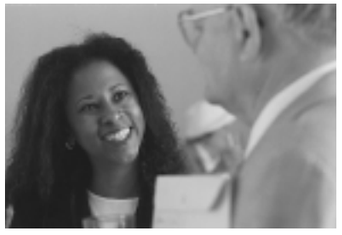
TOP Simran Singh took a patient's blood pressure during a medical screening at the Shrujan camp. Free medical and orthopaedics care were provided.

MIDDLE Simran Singh, David Litvak, Raj Krishnamurthy, Vivek Murthy, Shalini Kapur and Rupal Badani before their departure for Gujarat in March. Medical student Esther Choo joined them a day later. Another student, Rahul Rajkumar, helped organize the trip but was prevented from leaving by a family emergency.

BOTTOM Children such as these girls, dressed in the brightly colored garb typical of the region, were a main focus of the team, which organized an interim day program to provide some structure to their lives until schools could be rebuilt.

FOR 500 ALUMNI AND THEIR GUESTS, A RETURN TO NEW HAVEN

Congress Avenue Building, brain research, admissions process are the focus of 2001 reunion.



At this year's reunion, alumni donned hard hats for a tour of the Congress Avenue Building and put on their thinking caps for a seminar on admissions that asked them to decide the fate of a hypothetical medical school applicant.

More than 500 alumni and their guests attended reunion, which started Friday, June 1, with a discussion of the admissions process, a welcome from Dean David A. Kessler, m.d., and the traditional evening clambake. Across town, at the New Haven Lawn Club, alumni in public health were honored for their service to their communities.

The admissions discussion Friday afternoon in the Jane Ellen Hope Building included an interactive exercise that o=ered the audience a chance to review the qualifications of various applicants and make their own selections.

The next day discussion turned to "The Last Frontier: Understanding the Brain, Curing its Disorders," with a panel that comprised Bennett A. Shaywitz, m.d., professor of pediatrics and neurology and in the Child Study Center; Patricia Goldman-Rakic, m.d., the Eugene Higgins Professor of Neurobiology and Psychiatry and Neurology; Je=ery D. Kocsis, ph.d., professor of neurology and neurobiology; Dennis D. Spencer, m.d., chair and the Harvey and Kate Cushing Professor of Neurosurgery; and Stephen G. Waxman, m.d., ph.d., chair and professor of neurology. Topics ranged from dyslexia, including discussion of such famous dyslexics as Harvey Cushing, m.d., to memory loss and epilepsy.

At the alumni meeting that followed the brain symposium, Jocelyn S. Malkin, m.d. '51, right (top), received the Distinguished Alumni Service Award for her contributions as a teacher of students and residents, her advancement of the field of psychoanalysis and her commitment to the Association of Yale Alumni in Medicine.

Vincent T. Marchesi, m.d. '63, ph.d., below (bottom), director of the Boyer Center for Molecular Medicine, also received the Distinguished Alumni Service Award, for his commitment to Yale and his research into the proteins of the red cell membrane, discoveries that are featured in student textbooks.

Following the alumni meeting, Dean David A. Kessler, m.d., led alumni on a tour of the Congress Avenue Building, still under construction. Alumni climbed stairways to floors strewn with piping and wiring, while Kessler and John H. Bollier, executive director of facilities development and operations at the medical school, outlined the building's progress.

On Friday, the School of Public Health observed the Yale Tercentennial by honoring 50 outstanding alumni who have had exemplary careers in government or community organizations. The 50 were named to the *eph* Alumni Public Service Honor Roll at a luncheon at the Lawn Club in New Haven.

This year's Distinguished Alumni Award went to James Hadler, m.d., m.p.h. '82, director of the Connecticut Department of Public Health's Infectious Disease division for almost 20 years. "I have one of the best jobs in the world," Hadler said in his address to alumni. Although he acknowledged the "dark side" of working in government—the politics that sometimes interfere with programs—he said his work gives him "the ultimate reward, the feeling that what I do makes a di=erence to society."

1941

I want to thank the School of Medicine for a very pleasant 60th reunion this June. It is always nice to follow the development of the facilities of the school and, more important, the achievements of its graduates, particularly those of classmates. It was great, this year, to talk with **IRV WALTMAN** who, if I remember correctly, I had not seen since the day we were discharged from the Army in 1946.

I would like to thank the members of the Class of 1959 for their kind invitation to socialize with their group at the clambake, which I greatly appreciated.

PETER A. DUNCAN

1946

The highlight of our 55th reunion was the traditional gathering at Evelyn and **MARTY GORDON**'s beautiful home on Linsley Lake in Branford. As always, the refreshments were lavish and the entertainment began with videotapes from previous reunions as far back as our 40th. It convinced us that we haven't changed since then except, perhaps, in appearance. What Miki and Judy, child brides of **JIM KLEEMAN** and **TOM DOE**, thought of this is not recorded. We also saw a tape of **TIM BECK** receiving the "Human Condition" award from the Heinz Foundation, which led to other accolades since our last reunion, including **MARTY GORDON**'s Distinguished Service Award and leadership of the associates of the Medical Library and **VINNY LONGO**'s role in Pfizer's development of Viagra—fascinating!

Our guest of honor was **LEVIN WATER**'s widow, Priscilla Norton, who with Howard Spiro is writing a biography of Milton Winternitz, former dean of the medical school and promulgator of the Yale System. Vivid memories were evoked of "Winter" and his pathology course, and for some—**BILL BANFIELD**, **ELI WING**, and **BILL** and **MOLLY ALBRINK**—Winter's influence extended beyond our graduation.

Our memories of the World War II years were further sparked by a recording of our ASTP marching song, *MacNamara's Band*, which we received via **DON SHEDD** from the **NEVILLES**. The vocalist couldn't compare with our maestro, **TOM WHELAN**, but perhaps no one could! **DON SHEDD** polled the group to see how many of us wore hearing aids and, of those, how many were satisfied with them. The results would dismay the manufacturers of those gadgets! I was able to give our family pediatrician, **BERT FILER**, a favorable, 45-year follow-up on our four kids, who were among his earliest patients.

Those sending regrets due to illness or conflicting commitments were **FRANK BEHRLE**, **LINUS CAVE**, **GEORGE CUSICK**, **GREG FLYNN**, Mary Judd, Muriel Murphy, **JACK** and **LAURA NEVILLE**, **VINCE PEPE** and **BOB WAGNER**.

BILL WEDEMEYER

1951

We were a post-World War II class that lacked the homogeneity of pre-war cohorts at the School of Medicine and enjoyed a large diversity of age and life experiences. The majority were veterans of the armed forces who served overseas and attained ranks from private all the way up to colonel. Of 63 chosen to enter as first-year students, several dropped out early or altered course to pursue research and graduated with later classes. Fifty-two of us graduated in 1951, the last of Yale's "small" classes, and then dispersed across the USA to resume our war-interrupted lives.

Our 50th reunion began on a bittersweet note as we mourned and fondly remembered eight classmates who had died since our 45th reunion, which many of them attended. They were **FRANK ALLEN**, **MURIEL BAGSHAW**, **ELEANOR CLAY BIGLEY**, **SIDNEY FURST**, **SUMNER GOLDENTHAL**, **CARROLD IVERSON**, **ALFRED OWRE JR.** and **JOHN SULLIVAN**, who, as our secretary since graduation, best embodied the spirit of our class. Our condolences and best wishes go to their families.

Any classmate returning to Yale for the first time since 1951 must have felt like Rip van Winkle awakening! The growth of the physical facilities and the size, diversity and excellence of the faculty are awesome. Yale is well positioned to move the frontiers of research and patient care forward in the new millennium.

Our major activities during our reunion were renewing old friendships, reminiscing, sharing news of classmates unable to attend and listening to the excellent neurological sciences symposium and informative alumni association meeting. We applauded the award given to **JOCELYN MALKIN** for her contributions as a medical school alumni representative to the parent AYA and enjoyed meeting her mother and children, who were present. Classmates and spouses at the reunion were **TOM** and Barbara **AMATRUDA**, **PAUL** and Polly **BRUCH**, **JOHN FILLEY**, **LOWELL** and Ione **GOODMAN**, **BOB** and Sonia **HAMBURGER**, **AL** and Cecelia **KATZ**, **BILL** and Emily **KIEKHOFER**, **JOCELYN MALKIN**, **WALLY MORGAN**, **AL** and Donna **MOWLEM**, **JIM** and Jan **RILEY**, and **ANDY** and Irene **WONG**. The medical school administration and alumni association treated us like VIPs. We were their guests at both the spectacular clambake and the elegant reunion dinner.

JOHN GROEL, **BOB** and Dawn **ADAMS**, **JOHN** and Ruth **BERG**, **LARRY HARRIS**, **JOHN** and Mary Lou **HAXO**, and **BRAD** and Ruth **STRAATSMA** could not attend and expressed their regrets. **BRAD** was invited to be the opening-day speaker at an international congress of ophthalmology in Istanbul on the same date. We agree with his choice and send congratulations for the honor he received.

We left Yale Medical School with a renewed and increased respect for our school and the friendships we formed more than 50 years ago. Finally, on behalf of the class I would like to thank **LOWELL GOODMAN** for his efforts over many years as our class agent for the annual alumni fund drive

THE NAMES OF CLASS MEMBERS APPEAR IN **BOLD**.

and **ART PAVA** for chairing the 50th reunion gift fund. It is an always difficult and often thankless job to solicit money, no matter how important and wonderful the cause.

THOMAS T. AMATRUDA JR.

1956

For the Class of 1956 it was a great reunion weekend. Of the remaining 66 classmates, 24 came back to New Haven. We all agreed we caught the golden age of medicine and that Yale was the best possible entrance into that golden age. On Friday night the **DOWNINGS**, for the fourth time, hosted an elegantly casual buffet at their home in Guilford.

Saturday, the school's activities were capped by a formal banquet at the Quinnipiack Club. With most of the class in retirement, numerous addresses and invitations for visits were exchanged. The class wishes to thank Dean Kessler and the staff of the alumni office for their effort to make us feel welcome and have things run so smoothly.

Attendees included **LEVON** and Gloria **BOYAJIAN**, **ROSALIE BURNS**, **EDWIN** and Barbara **CHILD**, **JAMES** and Tina **COLLIAS**, **DON** and Leanne (MacDoughall) **DALESSIO**, **STEVE** and Helen **DOWNING**, **MITCHELL** and Janet **EDSON**, **GILBERT** and Rona **EISNER**, **TOM** and Carol **FERRIS**, **JOHN** and Arne **GARDNER**, **SUMNER** and Shayna **GOCHBERG**, **ROBERT GROVES**, **CHARLES** and Joan **HOPPER**, **MARY LOUISE** and Ken **JOHNSON**, **JEROME** and Linda **KLEIN**, **WILLIAM** and Gloria **LEWIT**, **PRESTON** and Jane **MANNING**, **DWIGHT** and Carol **MILLER**, **DONALD** and Anna Marie **NALEBUFF**, **FREDERICK NORTH**, **DAVID** and Eleanor **PAGE**, **ROBERT SCHEIG**, **JAMES** and Ruth **SCHEUER**, and **STANLEY** and Anne (Falk) **SIMBONIS**. Last-minute regrets were sent by **BOB** and Joan **HILL**, **GARY** and Karen **FRY**, **JOE** and Pattie **CERNY**, and **BILL** and Jane **O'BRIEN**.

DWIGHT F. MILLER

1961

Our 40th reunion went very well. Attendees included **VICTOR** and Laura **ALTSHUL**, **KENNETH** and Anne **ARNDT**, **EARL** and Kranie **BAKER**, **ROBERT** and Joyce **BRIGGS**, **DAVID** and Judith **BROOK**, **CHRIS** and Susan **DURHAM**, **JOHN** and Natalie **FENN**, **DAVID** and Marcia **GRIFFITH**, **BERNARD KOSTO**, Ellen Levy, **GEORGE** and Christa **LORDI**, **VINCENT** and Sally **MARCHESI**, **ANOUSH MIRIDJANIAN**, **ROLAND** and Grazina **PAEGLE**, **ELAINE PITT**, **WILLIAM** and Melba **ROGOWAY**, **ROY RONKE**, **SHAUN** and Millicent **RUDDY**, **ROBERT TAUB**, **FRANKLIN** and Lois **TOP**, and **WARREN** and Myra **WIDMANN**.

Ellen Levy presented to Yale the funds to endow a professorship, the **ROBERT LEVY** Chair in Preventive Cardiology. This substantial gift had been raised from family, friends and supportive companies.

Eight other classmates spent much time writing suggestions for a class seminar entitled "If You Had to Go to Medical School again, What Changes in the Curriculum Would You Recommend?" Their efforts culminated in a 22-page handout. Our alumni suggestions may help expand the horizons of the Educational Policy Curriculum Committee (EPCC) of the medical school. The committee consists nearly entirely of in-house academics. The four student representatives to the EPCC cannot be expected to be familiar with practice problems either. Since most Yale graduates eventually enter private practice, alumni advice is quite relevant.

VINCENT MARCHESI hosted the class meeting at the Boyer Center for Molecular Medicine on Saturday. It was noted that research and clinical practice have grown so much at Yale that support for teaching, although strong, has fallen behind. How to encourage good teachers became the topic around some class dinner tables at the Quinnipiack Club, and at Sunday breakfast, Lois and **FRANK TOP** suggested that our class contribute funds to reward excellence in teaching. Others pointed out that identifying a single best teacher of the year can be difficult and that a student survey may turn into a popularity contest. **VINCENT** suggested that alumni arranging to take a medical school class to dinner with their best teachers would provide more widespread recognition for the dedicated faculty. **BILL ROGOWAY**, our class reunion gift chairman, indicated to **ROLAND** that alumni could designate their donations also for the above-mentioned purposes.

ROLAND PAEGLE

1966

Practicing half-time, detesting airlines, having a pretty good car, early on Wednesday, May 30, I headed east with CDs of late string quartets of Beethoven and a lengthy audio book. Reached New Haven mid-afternoon Thursday. Walked a lot. Saw long-ago familiar buildings recycled. Gas stations seem to endure. Yale has not so subtly expanded.

Medical school tuition is now $30K per year, $50K with expenses. Wow! In nominal dollars my class got the whole package for what would buy a few months today. . . . Did we live in the golden age, or what?

Friday night, under holding sky, there was a clambake on the Harkness dorm lawn. Very pleasant. Lots of raw oysters and clams on the half shell. They must be medically safe. Overcooked steaks and perfect steamed lobster followed.

As I was slurping half-shell critters, I felt a hand on my arm. I glanced right. It took 200 milliseconds. Someone I had not seen in 35 years. I proclaimed, "**MARY ALICE**, you haven't changed a bit!" Wryly smiling, **MARY ALICE BERNET HOUGHTON** replied, "Neither have you!"

Saturday morning there were impressive presentations on neuroscience. From the behavioral to cellular to genetic level. Gee-whiz computer graphics. I recall how legendary Professor of Pathology Liebow had chalk and a blackboard, and a stick pointer as tall as himself to flail feckless interns who dropped the slides. Probably a good thing he didn't have a laser.

Saturday evening the class dinner was held at an Italian restaurant on the outskirts of New Haven's Little Italy, in the shadow of Interstate 91, unpretentiously named Adriana's Restaurant. It turned out to be very nice. Mythic thirteen sat at table.

During the early part of dinner, who should show up but Dean Kessler accompanied by two keepers, ladies from the alumni office. It reminded me of our beloved president, also with a Yale connection, making the rounds of inaugural balls.

The members of the class of '66 (Latin, sextiest-sex), no shrinking violets, offered opinions and observations. The dean was reminded that he was going to have to feed that really big building. And, was he doing the new graduates and the world any favor by sending the newbies out on graduation day $100K negative?

At dinner, and before, various class members briefly recited their current status.

As I heard it:

REY SPECTOR, after a distinguished (**REY** is modest; this is my estimate) career including the University of Iowa and Merck, is now semi-retired with several medical school appointments. He is building a dream house in Colt's Neck, N.J. He and wife Michiko are currently having a memorable motel stay while getting a hard-knocks course in contractor delays and cost overruns. If anyone has a magic answer, **REY** is having cervical and lumbar disc problems and getting fed up with conservative therapy.

JOHN and **MARIAN MATHEKE MELISH**, in from Honolulu, report that everything is not heavenly in paradise. Even though Hawaii has a unique health care funding system, gaps abound, and it sounds like they work pretty hard. When I mentioned to **JOHN** some roof leaks I had this past winter, I was told Hawaii has industrial-strength termites that specialize in eating roofs. **MARIAN** also reports football linesman cockroaches play soccer with full size ball in kitchen late at night.

MARY ALICE BERNET HOUGHTON and husband Bill (M.D. '64) are both still practicing psychiatry in Milwaukee. I understand psychic insight is little help in raising children, and traditional methods (scream and kickass) were used.

ARNE YOUNGBERG, senior radiologist in his group in Waterbury, is the group mammographer. He expects to hang it up in the near future. He was especially looking forward to a fishing trip in Patagonia.

PETER GIBBONS, with wife Christina, was here. He is a radiologist in Brattleboro, Vt. He noted radiology, long somnolent after sunset, has become increasingly 24-hour, a significant burden.

JIM BROWN, in medical oncology, from Middletown, also dropped in with wife Pat for the last night's dinner. He looks five years older than he did in 1966. Still going strong.

EUGENE P. CASSIDY

1971

The 30th reunion of the Class of 1971 was attended by 29 of our class members: Drs. **CATES**, **COHN**, **COSSMAN**, **EISENFELD**, **FOSTER**, **GARDNER**, **KINDER**, **KLEEMAN**, **KLEIN**, **KRINSKY**, **LIPPMAN**, **MENDEN-REESE**, **MILLER**, **MILLS**, **MINIHAN**, **MOGGIO**, **MORGAN**, **PATTI**, **PERLMAN**, **RAND**, **RAPHAEL**, **RINZLER**, **STEWART**, **TRAVERS**, **TSALBINS**, **VAUCHER**, **VIGNOLA**, **WEIHL** and **WOODHEAD**. The class dinner was highlighted by Dr. **FOSTER**'s sartorial creativity and the dean's visit. It is not true that Dr. Kessler was seen smoking on the 17th green.

BARBARA KINDER graciously invited us to her lovely Branford home for a delicious brunch. **ALICE O'NEILL** was lovingly remembered and an initiative for an annual lecture in her honor was discussed. **JOAN MENDEN-REESE**, a Brown/ Pembroke classmate, will share this idea with Alice's family. **DAVID LIPPMAN**, unable to attend the Saturday dinner because of his daughter's graduation, gave yet more puzzles to ponder. The solution to the puzzle—what do the words pact, vandal, floral, calamari, Coca-Cola, etc., have in common?—is that they are composed exclusively of the two-letter state abbreviations, e.g., pact = Pennsylvania (PA) + Connecticut (CT). An unanswered query is what common medication can also be so composed. The answer will be given at the 35th reunion. See you there.

DAVID LIPPMAN

1976

Outstanding 25th reunion, a tribute to the vitality and youthfulness of our class! Delightful Friday night clambake, Saturday lunch and filled-to-capacity, delicious Saturday dinner at Zinc. Classmates and family came from as far away as Buenos Aires (**RICHARD LOW**) and California (**DVORA CYRLAK**, **RANDY HAWKINS** and **SUSAN RYU**).

Attending were **SARAH AUCHINCLOSS** (private practice psychiatry, NYC) and son Andrew; **ALFREDO AXTMAYER** (private practice orthopaedics, Wallingford, Conn.), wife Pat and daughter Caitlin; **SHARON BONNEY** (associate director clinical research, Pfizer, New London, Conn.) and husband Jim; **FLORENCE COMITE** (Concentric Medicine, New Haven) and partner Jonathan Goldstein; **DVORA CYRLAK** (professor of radiology, University of California at Irvine) and husband Neil; **VINNIE DICOLA** (private practice cardiology, New Haven); **KEN DOBULER** (chair, Department of Medicine, Griffin Hospital, Derby, Conn.) and wife Sue; **TODD ESTROFF** (psychiatry, Atlanta); **STEPHEN GOLDFINGER** (psychiatry, New York); **ROSE GOLDMAN** (director of occupational and environmental health, Cambridge Hospital, and associate professor at Harvard) and husband Alan; **RANDY HAWKINS** (private practice neurology, San Diego) and wife Penny; **RICHARD KAYNE** (private practice endocrinology, Cheshire, Conn.) and wife Maria; **NORM KOHN** (private practice psychiatry, Chicago); **BILL LEVY** (private practice cardiology, Abington, Penn.) and wife Karen (M.D. '77).

Also, **RICHARD LOW** (CEO, Infor*Med Corp., Buenos Aires and Woodland Hills, Calif.) and wife Isabel; **SID MANDELBAUM** (ophthalmology, NYC) and wife Diane Oshin; **CINDY MANN** (private practice pediatrics, Hamden, Conn.); **DOUG MANN** (private practice ENT, Media, Pa.); **RICH PELKER** (professor of orthopaedics, Yale); **SUSAN RYU** (ophthalmology, Palo Alto, Calif.); **LARRY SAMELSON** (chief, Laboratory of Cellular and Molecular Biology, NCI); **RICHARD SCHOTTENFELD** (professor of psychiatry, Yale, and the new master of Davenport College); **PETER SWANSON** (family practice, Shelton, Conn.); **CHARLIE SWENSON** (associate professor of clinical psychiatry, University of Massachusetts); **BOB TAYLOR** (oncology, Milwaukee); **PETER TING** (anesthesia, Dover, Mass.); **JOHN WILES** (private practice dermatology, New London, Conn.) and wife Joan; and **CAROL ZIMINSKI** (associate professor of medicine, Johns Hopkins) and husband Terry.

Classmates responding but unable to attend were **BILL BITHONEY** (physician-in-chief and chair of pediatrics, St. Joseph's Children's Hospital, Paterson, N.J.); **ROGER BOSHES** (assistant professor of psychiatry, Harvard at Fall River, Mass.); **HELEN CHANG** (private practice ob/gyn, Poway, Calif.); **JOSEPH CIABATTONI** (retired this summer from internal medicine practice, Rhode Island); **JOHN CLEMENS** (director, International Vaccine Institute, Seoul, and husband of classmate **BONNIE STANTON**); **CANDACE CORSON** (lecturer on nutritional medicine, Granger, Ind., and married to George Knowles, M.D. '75); **MARK CULLEN**

(professor of medicine and public health and director of occupational medicine, Yale); **JOHN ELEFTERIADES** (professor and chief of cardiothoracic surgery, Yale); **CAROL EPSTEIN** (co-founder, MediVector Inc., Cambridge, Mass.); **RICHARD FRANK** (private practice psychiatry, Milwaukee); **IRA GEWOLB** (professor of pediatrics, University of Maryland); **GLENN HARDER** (retired from private practice of plastic surgery in 1992, Weston, Mass.); **PAM HERBERT NAGAMI** (internal medicine and infectious disease, Southern California Permanente Medical Group, Woodland Hills, Calif., and married to Glenn Nagami, M.D. '78); **CLARION JOHNSON** (medical director, Exxon Mobil, Fairfax Va.); **DAVID KAWANISHI** (private practice cardiology, Mission Viejo, Calif.); **RICHARD KREMER** (CEO, Forward Associates, consulting in health care claims and negotiating facility fees, Williamsburg, Va.); **CAROL LEE** (professor of radiology, Yale); **DAN RAHN** (as of June the president of Medical College of Georgia, Augusta); **NORM RIZK** (professor of medicine, director of medical ICUs and senior associate dean for research, Stanford); **DAN SCHUSTER** (professor of medicine and radiology and associate dean for clinical research, Washington University); **DIRK SOSTMAN** (professor and chair of radiology and senior associate dean for clinical affairs, Cornell); **BONNIE STANTON** (chair of pediatrics, West Virginia University, Morgantown, and married to classmate **JOHN CLEMENS**); **JACK TAUBER** (private practice orthopaedics, Beverly Hills); and **JERRY ZELDIS** (chief medical officer, Celgene Corp., Warren, N.J.).

Excellent to share the weekend with so many of you and to see that we are thriving in life and our careers. Our camaraderie remains great, and I hope that we can keep in contact and succeed in seeing each other more often. Start planning for the 30th reunion now! Many thanks to my wife, Maria, who did almost all of the reunion work for us.

RICHARD KAYNE

1981

The good news is that we had a wonderful time and everyone in our class looks the same as we did 20 years ago. The weekend was a little wet, but that did not prevent us from catching up and sharing the events that have occurred in our medical and social lives.

DAVE LEBWOHL was there the first night for the clambake. He lives with his wife and two children in Connecticut. **DAVE** is working on drugs similar to Tamoxifen for cancer treatments. **ERIK FISHER**, always kind and understanding, runs a county psychiatric clinic in Oregon for the severely mentally ill. He believes that multidisciplinary practice is the best way to treat such patients and he works towards teaching them to live independently. He and his wife live in Eugene and he bicycles to work. **DAVID GENDELMAN**, his wife, Deborah Zuckerman, and I are hoping to coordinate our families to meet on a bicycling trail in Lexington, Mass. **DAVE** is an ophthalmologist working at Mass. Eye and Ear and his wife is a dermatologist. They have two boys and a girl (Isaac, Hannah and Jacob) and a very quiet household no doubt. **DOVELET SHASHOU** is also an ophthalmologist, specializing in pediatrics at Manhattan Eye and Ear. She drove up from New York with her husband, Jonathan Trambert, who is an interventional radiologist. They have two children — Steven, 11, and Emily, 8. **LISA BABITZ** and **STEWART GREISMAN** work in Manhattan. They took over **STEWART**'s father's internal medicine practice after completing their residencies at Yale-New Haven. She specializes in geriatrics and he in rheumatology. **LISA** was the second resident at Yale to have children during the residency. Her oldest is Laura, 17, followed by Jill, 13, and Jack, 9. **BARBARA ROACH** and Rick Carroll are in practice at Yale-New Haven. Both are rheumatologists. They have two children, Mathew, 13, and Emily, 10. They live in Hamden. **CYNDY** and Raymond **ATEN** were both in attendance. **CYNDY** has most recently practiced medicine at Yale and Wesleyan and is opening a private practice in New Haven. They are perhaps the first grandparents in our class. Hopefully we will all have that wonderful experience. **DAVID LU** and his wife, Susan, are now living in **DAVID**'s hometown (and mine), Washington, D.C. **DAVID** is a cardiologist and has three children, Bobby, 15, Becky, 14, and Mathew, 7. He seemed happy and prosperous. **BILL HUNT** has not lost his sense of humor. He attended the reunion with his wife, Jan. He is in private practice in neurology at Bridgeport Hospital. They have three children, Diane, 14, Stephen, 12, and Gregory, 10, all with great nicknames. **CHARLES SHANA** is a gastroenterologist in Newport, R.I., and Fall River, Mass. He has a lovely wife, Miriam, and two children, David, 10, and Philip, 8. **PAT BURKE** is married to Jolin Proffitt and is home with her 8-year-old twin boys. She is an internist and they reside in Downes Grove, Ill.

I am still recovering from the fact that I graduated from medical school 20 years ago. I admit the students that I spoke to did look young. I am a surgeon at the Brigham and Women's Hospital, where I specialize in the treatment of breast cancer. I am married to Randall Kennedy, J.D. '82. We have three children, Henry, very 6, and Rachel and Thaddeus, both very two and a half.

I see and hear about lots of our classmates from time to time. **TROY BRENNAN**, **TOM KUPPER**, **DON INGBER** and **JOAN BENGSTON** all roam the halls at this institution. I have also heard great things about **ADA ADIMORA**, **JUANITA MERCHANT** and **JANE ASCH**. I am hoping this letter will entice them and others to attend our next reunion. Goodbye for now.

YVEDT MATORY

1986

The Class of 1986 reunion welcomed **DANIEL FIERER**, **JEREMY HOLTZMAN** and his wife, Janet Mills, **DAE** and Judy **SONG**, **ERIC** and Pamela **SUAN**, **CATHARINE ARNOLD**, **ROBERT KINNEY**, **ROBERTO LEWIS-FERNANDEZ** and his wife, Maria Almeida, **JOHN** and Caroline **WYSOLMERSKI**, and **BETTY KLEIN** back to New Haven. Food and drinks were again the starting point for reliving stories of anatomy lab, practical jokes and softball games, catching up on current news and sharing gossip of classmates unable to attend.

DANIEL is in NYC focusing on AIDS research at Mount Sinai. **JEREMY** continues his work in internal medicine and health care research at the University of Minnesota. Ophthalmology was well represented this year. **DAE** has started his own private practice in general ophthalmology in Selma, Ala. **ERIC** is in private practice in Baltimore, specializing in the retina. **BETTY**, our reunion chair, also specializes in the retina in Redding, Conn. **CATHARINE** is balancing her career in rheumatology with shuttling her kids to various activities in Guilford, Conn. **ROB** has the most sane position of all, serving as medical director for an insurance company in Hartford. **JOHN** remains on the faculty at Yale in the endocrine section of the Department of Medicine. **ROBERTO** has returned to the mainland from Puerto Rico, practicing psychiatry at Columbia Presbyterian in New York.

The most refreshing conclusions over the weekend were that none of us has changed a bit in outward appearance — although inside we are all a lot wiser. The group's major regret was that we did not see more classmates in attendance. For 2006, if you are not here to deny rumors, rumors will turn into truths! Hope to see you all for the 20th in 2006!

ERIC P. SUAN

1991

The Class of 1991, regarded by some as Yale's greatest, reunited with characteristic largesse in numbers and spirit. While many were able to be at the Friday evening clambake, all attended the dinner on Saturday night, which was held at Chateaux Leaubeau. In attendance were **PETER BERNSTEIN** and wife Cathleen Barnhart; **ELIZABETH BOWER** and daughter Mara Leo; **MARCUS BUTLER** and partner Christopher Yulo; **CYNTHIA CARVER SMITH** with husband David Smith and family; **DOUG FLEMING** with wife Robin Buckingham and family; **DAVID FRANKFURTER** and family; **WENDY GRANT** with her husband, Steve Bowers, and son Ian; **JEANNE HAIMOVICI ACKMAN** with husband Robert Haimovici and family; **CARL** "The Good" **HENNINGSON**; **LARRY HIRSCH** and Gaetane Francis; **LIZ HOLT**; **DORIS IAROVICI** with husband Larry Katz; **JOHN KILTY** with wife Pat Janowski and young Joe Kilty; **TOM LIN**; **PETER MARCUS** and wife Lyree (family back home in Indiana); **FUNDA MERIC**; **JANE MINTURN**; **MEG STEVENS O'NEILL** and husband Michael; **MARC POTENZA** and wife Susan Smith; **LIZ ROTH**; **DAN SAAL** (family back home in California); **JEFF SCHECHNER** and wife Christina Herrick; **LAURIE SHAKER-IRWIN**; **JAMES STANISLAW** and wife Alicia (family back home in North Carolina); **STACY BELLER STRYER** and husband. Dan Stryer (M.D. '90, poor fellow); **DAVID UTZSCHNEIDER** and wife Gordana, with young Niki and Eva; and **MARCO VERGA** with wife Wendy. In addition, we were honored by a visit from Dr. Morris Dillard, whom many of us knew and loved as director of the Wednesday Evening Clinic. Messages with regrets came from **MARC AGRONIN** (whose envelope art ensured that everyone opened their invitations), **DARYL DANIELS**, **RICK IHNAT**, **ANN DENEHY SMITH**, **BOB SPILLANE**, **SYMPHOROSA WILLIAMS**, and, just now, **JIM HICKS**. Last-minute regrets came from **KENT MIN** and **ELLEN MARKSTEIN GELLER** and husband David. **COLLEEN FOY** could not make it but sent e-mail photos (which presided over the kitchen Saturday night) of herself with husband Craig Sterling and their young son. And **STEVE UGENT** revived the "Uge, Uge, Uge" chant during a hilarious telephone call Saturday afternoon.

Finally, I must thank the Office of Alumni Affairs for making the dinner at my house possible and for arranging catering from the incomparable Adriana's Restaurant, one of New Haven's greatest culinary gems. I think it fair to say that everyone had a fabulous time at reunion. They seem to be getting better exponentially. So start thinking now about 15!

FRANCIS M. LOBO

1996

This year's fifth reunion class had a bumper crop of attendees. Many were still in New Haven doing residencies and fellowships. However, our congratulations go to **WOLFFE NADOOLMAN**, who came all the way from Berkeley, Calif., to join the gang. Both of the **POGGI**s came with their lovely 3-month-old daughter, Eliza. Those of us who have not yet attempted parenthood, such as **KATHLEEN FIGARO** and **LYNNE STRASFELD**, fellows in NYC, had impromptu lessons on holding and soothing this open and elegant infant during the clambake. She and **REBECCA CRICHTON** and **SIMON CORNELISSEN**'s infant son were pictured together in what could be the youngest second-generation pairing of the class of 2026. **RANYA HARVEY**, who made a brief visit to the clambake, is now a practicing pediatrician. **PETER FERREN** had come back to New Haven to do a fellowship at the Yale Child Study Center before possibly heading back to Atlanta. **JON GRAUER** and **JOHN BEINER**, both orthopods at Yale, and **JEFF MEYERHARDT** hung around, much like old times. **JULIE (ROTHSTEIN) ROSENBAUM** came with her husband, and **SUSAN TRUMAN** and husband brought their two children. **LISA SANDERS** did not bring her little ones to dinner. **SARAH CLEVER**, who is now an RWJ Clinical Scholar at U. of Chicago, breezed in late to reunion in order to finish recruiting some patients to her most recent study. She and I took in the tour of the Yale Center for British Art and had great fun.

The dinner at the Graduate Club, where we were sponsored by the 50th reunion class, was lively and intimate. We sat at two tables and discussed the difficulties of our residencies and our hopes for the future. In a surprise move, **NG HO**, who had been an ER resident, decided to become a Wall Street mogul and is now in the e-health section of drug giant Pfizer. Not so surprisingly, **OWEN GARRICK**, who was not there, is also on Wall Street at Goldman Sachs, also in the technology sector. **NG**'s husband, actually Class of 1995, came to dinner with us. He is now a chief resident in plastics at Yale. **MARTY MAYSE**, a fellow at Yale, also came. **MONICA MEDYNSKI** sat glowing next to her new husband, Neil, previously a Yale radiology resident, happy with her choice of radiology. Most of us seemed quite content with our choices in medicine, and many of us look forward to our next reunion when we can see each others' families growing.

People we missed: Although these people were in New Haven, they did not make the reunion and were sorely missed. **DUANE BRYAN** is currently a physician at Yale Community Health Clinic, and **BASEM JASSIN** is finishing his surgical residency, as is **TONY PHAM**. **DAVID KIM** is a radiation oncologist. **DANA LOO** is a chief resident of medicine; **JAVIER DAVILA** is also in medicine at Yale. Most of the New York crowd did not make it: **TIM JOHNSON** is currently finishing up ortho at Hospital for Special Surgery; **RACHEL VILLANUEVA** and **CLARA LEE** are conquering ob/gyn and surgical residencies, respectively, at New York Presbyterian. **LILLIAN OSHVA** has finished ER at Bellevue, where she is now an attending doing clinical research. **DAVID LEE** and **EVERETT HSU** are both married and living in California. Where are you, **NELSON**?

KATHLEEN FIGARO

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For more photos from Alumni Reunion Weekend, please visit our website and select EXTRAS.

NOTES

1960s

JOSEPH F.J. CURI, M.D. '64, reports that he is "still in a solo pediatric practice after 31 years. My son, Michael, received his M.D. from UConn and is in a pediatric residency in Virginia. Anne has put her Harvard law degree aside and is a professional duo-athlete. Sarah, a part-time lawyer, is getting her M.P.H. at Harvard. Katheryn is studying for her M.A. in mental health counseling and is a professional mountain biker in Vermont. I thoroughly enjoyed representing the medical school at the Tercentennial weekend."

RALPH S. GRECO, M.D. '68, HS '73, was appointed the Johnson & Johnson Distinguished Professor and chief of the Division of General Surgery at Stanford University School of Medicine, where he is also director of the General Surgery Training Program. After completing his surgical training at Yale, Greco spent two years in the U.S. Army Medical Corps in Seoul, Korea, and Fort Meade, Md., and then joined the faculty at the former Rutgers Medical School. He became a full professor there in 1983, three years before the school changed its name to the Robert Wood Johnson Medical School. Greco was appointed chief of surgery at Robert Wood Johnson University Hospital in 1996. His clinical interests include pancreatic surgery, surgical oncology and endocrine surgery. He has long pursued research directed at elucidating the response of host cells, namely neutrophils, to nonbiological surfaces utilized in biomedical implants and devices. Greco, his wife, Irene Wapnir, M.D., and their three children moved to Palo Alto, Calif., in August 2000.

AUGUSTUS A. WHITE, HS '66, was recently appointed master of the Oliver Wendell Holmes Society, one of four academic societies at Harvard Medical School. As master, his goal is to help educate students to be excellent scientists and clinicians who will provide compassionate care to all of their patients, while preserving their own well-being in order to serve happily for many years. White, who focuses on the spine, is a professor of orthopaedic surgery at Beth Israel Deaconess Medical Center and a member of the Health Sciences and Technology faculty at Harvard Medical School. He also served as orthopaedic surgeon-in-chief at Beth Israel Hospital for 13 years. The American Orthopaedic Association honored White in June in Palm Beach, Fla., by naming him the Arthur R. Shands, Jr., Lecturer, for outstanding contributions to the orthopaedic profession. He delivered a lecture titled "Our Humanitarian Orthopaedic Opportunity," in which he described the serious racial disparities in health care in the United States, which he attributed to racial bias. He spoke about the history of this phenomenon and challenged his audience to try to eliminate health care disparities for society's well-being.

1970s

MICHAEL L.J. APUZZO, M.D., HS '73, received the William Beecher Scoville Prize from the World Federation of Neurosurgical Societies at the opening ceremonies of the September 2001 World Congress in Sydney, Australia. The prize is awarded to a neurosurgeon who has made a principal contribution to the art and science of neurosurgery on an international scale. William Scoville was a Yale neurosurgeon who made numerous contributions and innovations in the field while being active in globally organized medicine. Apuzzo was a pupil of Scoville's and is now the Edwin M. Todd/Trent H. Wells, Jr., Professor of Neurological Surgery and Radiation Oncology, Biology and Physics at the Keck School of Medicine of the University of Southern California in Los Angeles. He was honored for his work in introducing modern aspects of cellular and molecular biology to the operative armamentarium, as well as for his advocacy of the international exchange of ideas and unified global education.

ATTILIO VINCENT GRANATA, M.D. '77, an associate clinical professor of medicine at Yale, was elected to the board of directors of the Citizens for Patients' Rights at the group's July 19 meeting. Citizens for Patients' Rights is a grassroots organization dedicated to educating and empowering the public to deal with problems in the health care system. In addition to his academic practice, Granata is a consultant to a number of national and international clients on health care issues, such as strategic planning, cost-effectiveness analysis and quality-of-care planning. He is president and CEO of Health Care Consulting Practice in Orange, Conn. Granata served his residency in internal medicine at Stanford University Medical Center and also completed an M.B.A. as a Palmer Scholar at the Wharton School of the University of Pennsylvania in 1994. He serves on the Health and Public Policy Committee of the American College of Physicians.

In a biographical sketch for the Centers for Disease Control and Prevention (CDC), **DANIEL A. POLLOCK**, M.D. '79, described a change in his career as follows: "In my work [as an emergency physician], I saw the same injury types again and again and again. As a result, I thought it would be important to learn injury demographics and causes, and to find ways to prevent injuries, instead of continually treating them and trying to limit their effects." This conviction led him from a position as an instructor of clinical medicine at New York University School of Medicine to a stint in the Epidemic Intelligence Service of the CDC in 1984. For two years, he worked on the Agent Orange Projects. He then continued within the CDC to become the team leader of the Acute Care Team within the National Center for Injury Prevention and Control (NCIPC). Since 1999, he has served as the acting director of the NCIPC's Division of Acute Care, Rehabilitation Research, and Disability Prevention, which provides national leadership in preventing and minimizing the impact of nonoccupational injuries. His goal is to engineer a shift in the way medicine is taught and researched toward a population orientation that includes prevention and complements the clinical approach of treating one patient at a time.

1980s

INA S. CUSHMAN, PA '86, was elected president of the American Academy of Physician Assistants. She has held a variety of other positions within the organization in the past. She is a senior physician assistant with Harvard Vanguard Medical Associates, a private practice group providing HMO as well as fee-for-service care. Cushman works out of the Braintree, Mass., center, but consults and teaches throughout the organization and around the country. She pioneered a nationally recognized wound care program and contributed three chapters to the second edition of *Telephone Medicine: Triage and Training for Primary Care*. She was also honored by United Airlines for her treatment of a fellow passenger in cardiac crisis.

MICHAEL SIMONS, M.D. '84, HS '87, has been appointed the Anna Gundlach Huber Professor of Medicine and chief of the Section of Cardiology at Dartmouth Medical School. He moved to Dartmouth from Harvard Medical School, where he was an associate professor of medicine and director of the Angiogenesis Research Center at Beth Israel Deaconess Medical Center. Simons transported his entire lab northward, including almost 20 researchers and $2 million a year in funding from the National Institutes of Health, the American Heart Association and industry sources. His research in angiogenesis focuses on the use of a growth factor called PR39 to stimulate blood vessel growth.

SEND FACULTY NEWS TO
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DONALD J. COHEN, M.D. '66, director of the Yale Child Study Center and Sterling Professor of Child Psychiatry, Pediatrics and Psychology, died October 2 after a year-long illness. He was 61.

Cohen graduated from the School of Medicine in 1966, joined the Yale faculty in 1972, and in 1983 became director of the Yale Child Study Center. Under his leadership the Child Study Center became internationally recognized for its multidisciplinary programs of clinical and basic research, professional education, clinical services and advocacy for children and families. Cohen's clinical and research activities focused on developmental psychopathology of the serious neuropsychiatric disorders of childhood, including autism, pervasive developmental disorders and tic disorders such as Tourette's syndrome. His leadership in the study of the impact of violence on children and families created a worldwide network of collaborators.

Cohen published more than 400 articles, chapters and books. He served as president of the International Association of Child and Adolescent Psychiatry and Allied Professions, chair of the publications committee and vice president of the Board of Governors of Yale University Press, co-chair of the Child Health and Development Institute, international president of the Telefon Azzuro Foundation in Italy and chair of the international advisory committee of the Schneider Children's Hospital of Israel.

He was a member of the Institute of Medicine of the National Academy of Sciences and a training and supervising psychoanalyst at the Western New England Institute of Psychoanalysis. He received numerous awards, including an honorary degree in 1997 from Bar-Ilan University in Israel for his commitment to child psychiatry and the mentorship of young professionals in Israel, a Special Presidential Commendation from the American Psychiatric Association and a Lifetime of Research in Autism Award from the National Alliance for Research on Schizophrenia and Depression.

KENNETH COLBY, M.D. '43, a psychiatrist and a pioneer in artificial intelligence and computerized therapy, died on April 20 at his home in Malibu, Calif. He was 81.

In the early 1970s, Colby led a team that developed the software program Parry, which was designed to imitate the conversation of a paranoid schizophrenic. In test interviews, psychiatrists were unable to distinguish Parry's responses from those of real paranoiacs. Parry was the only program to pass the "Turing test," meaning that it could successfully impersonate a person in a typed conversation.

In 1989, Colby and his son, Peter, founded Malibu Artifactual Intelligence Works to develop therapeutic software. One program they designed was called "Overcoming Depression," and it combined a text-based tutorial, cognitive therapy techniques and a free-association component. The program was used by the Department of Veterans Affairs, the Navy and Kaiser Permanente, among others, to reach people with mental illness who do not seek professional help.

Colby was born in Waterbury, Conn., and graduated from both Yale College and the School of Medicine. He practiced psychiatry for 20 years, and then was a professor of computer science at Stanford University, where he created Parry at the university's Artificial Intelligence Laboratory. He moved to UCLA in 1974 to work in the psychiatry and biobehavioral sciences departments. He retired from academia in 1989, when he started Malibu Artifactual Intelligence Works. He published 10 books and over 100 articles in the fields of psychotherapy and artificial intelligence. He also wrote two books about chess and was a highly rated player.

DONALD W. DEWALD, M.D., HS '41, died January 13 at MedCentral/Mansfield Hospital in Ohio. He was 86.

Dewald trained as an intern and resident at Yale School of Medicine after graduating from Case Western Reserve University School of Medicine, where he received the Hoover Scholarship as valedictorian. He was a teaching fellow at Case, and then enlisted in the Army during World War II. He attained the rank of major and was chief of the medical service at Pasadena Regional Hospital in California.

Starting in 1946, he practiced medicine in Mansfield, 21 of those years with his son. Dewald was on staff at MedCentral/Mansfield and Peoples Hospitals and was a past president of the Richland County Medical Society.

LAWRENCE A. DOWNS, M.D. '64, a psychiatrist and one-time Yale basketball star, died on May 20 at his home in New London, N.H., after a long illness. He was 65.

Born in Indianapolis and raised in White Plains, N.Y., Downs later spent time as an English-speaking Union Fellow at Brighton College in Sussex, England. He came to Yale with the Class of 1959 and made the All-Ivy Basketball Team.

He went on to the School of Medicine and then a residency in psychiatry at New York Hospital. He joined the faculty of Cornell Medical College and also served as the liaison psychiatrist at Memorial Sloan-Kettering Cancer Center. At the same time he maintained a private practice in both New York City and New London, N.H., until his retirement in 2000.

PAULA YANEY GAMBILL, M.P.H. '77, a recruiter and consultant to the health care industry, died in April 2000 after a prolonged illness.

After receiving her M.P.H. in 1977, she worked from 1981 to 1983 in the health and medical division of Booz, Allen & Hamilton, and then was a special assistant to the managing director of APM Inc. In 1987, she started work at Empire Blue Cross and Blue Shield and advanced from a program evaluation and development specialist to a manager of professional services utilization review. In 1993, she rejoined APM Inc. as a manager of senior recruiting.

ROBERT I. HINKLEY, M.D. '44, a general practitioner in Groveton, N.H., died on April 13 at the Morrison Nursing Home after a brief illness. He was 81.

Born in Lancaster, N.H., Hinkley graduated from Bowdoin College in Maine and then received his M.D. from Yale. He did an internship at Worcester City Hospital in Massachusetts from 1944 to 1945 and then served two years in the Army as a post surgeon at the Ogden Ordnance Depot in Utah. He attained the rank of captain.

On returning from the military, he settled in Groveton and remained there for the rest of his life. He started a general practice in 1947 and was on the staff of Weeks Hospital until his retirement in 1984. He developed the first cardiac care unit at Weeks. He was also president of the staff for two years and was on the hospital's Board of Trustees.

Hinkley was widely involved in local health care and government. He was a member of the New Hampshire Medical Society and served two years as president of the Coos County Medical Society. He was also elected a charter fellow of the American Academy of Family Physicians in 1975. He was appointed to the New Hampshire Milk Sanitation Board by the governor. For many years, he was the Groveton and Stark health officer, and he also served on the Groveton school board for nine years. He was a trustee of the York Educational Foundation and director and president of the Groveton Foundation. Additionally, he was a senior master in duplicate bridge and shot golf rounds in the 70s in each of seven decades.

R. LEONARD KEMLER, M.D. '43, a clinical professor of surgery at the University of Connecticut School of Medicine and a distinguished thoracic surgeon, died on May 20 in Boston from leukemia. He was 82.

Kemler was born in Hartford, Conn., where he would return to practice for the majority of his professional life. He received a B.A. and an M.D. from Yale, and then did his internship and residency at the Barnes Hospital in St. Louis, where he trained under Evarts Graham. He served in the Navy in World War II as a lieutenant in Shanghai, China. He was also a ship's surgeon aboard the USS Estes.

He returned to Hartford to start a private practice in cardiovascular thoracic surgery in 1950, and was the founding president of Cardiovascular and Thoracic Associates P.C. He joined the faculty of the University of Connecticut School of Medicine and also became a professor of biology and a member of the Pre-Med Advisory Committee at the University of Hartford. He was a staff member at Cedarcrest Hospital, past director of cardiovascular thoracic surgery at Mount Sinai Hospital, senior attending thoracic surgeon and director of cardiovascular and thoracic surgery at New Britain General Hospital, and a member of the Department of Surgery at Hartford Hospital.

He received the Chairman's Award of the Yale Alumni Fund, as well as the Silver Bowl Award and the Distinguished Alumni Service Award of the Yale University School of Medicine Alumni Fund Association.

ANITA G. PEPPER, M.P.H. '60, PH.D. '72, a professor emerita at St. Louis University and an advocate for improving public health by bettering the services available to all people in society, died on April 7 of cancer at her home in Montague, Mass. She was 73.

A native of New York, Pepper graduated from Smith College and the New York School of Social Work. She worked as a caseworker for the Jewish Family and Children's Agency in Chicago and as a psychiatric social worker at the Bronx Municipal Hospital/Albert Einstein School of Medicine. She completed her M.P.H. at Yale in 1960. She joined the EPH faculty and became the special assistant to the dean of the School of Nursing. She helped prepare the school's prospectus and gained her PH.D. in 1972.

After leaving Yale, she headed a new social work and health service training program at Washington University. In 1976, she became a professor of epidemiology at St. Louis University's school of nursing. According to a former student, she was a strong advocate for improving health care services to the poor of St. Louis, as well as for maternal-child health. She and her husband, Max Pepper, M.P.H. '59, helped to form the organization Health Care Is a Human Right.

She retired from St. Louis University in 1989 and moved to Montague, Mass., but she continued to lecture at universities and hospitals. She held a clinical professorship at Tufts University School of Medicine and an adjunct position at the University of Massachusetts at Amherst.

DAVID H. RIEGE, M.D. '46, a pediatrician, died on October 11, 2000, at Lawrence and Memorial Hospital in New London, Conn. He was 80.

Riege was born in Springfield, Mass., and raised in Longmeadow, Mass. He graduated from Wesleyan University and Yale School of Medicine. He was on the staff of Hartford Hospital from 1952 until 1984. He practiced pediatrics in West Hartford, Conn., where he also lived and raised his family, retiring in 1984.

JESSE G. RUBIN, M.D. '57, a clinical professor of psychiatry at George Washington University and a co-founder of a large chain of psychiatric hospitals, died May 25 of prostate cancer at his home in Washington, D.C. He was 68.

Rubin and a group of other psychiatrists founded Psychiatric Institutes of America, a corporation that at one time oversaw 1,000 hospital beds in 10 states. He acted as medical director for the company from 1970 to 1973 and 1978 to 1983. He also helped to establish a nonprofit institution, the Psychiatric Institute Foundation, which supported privately run community services, including a halfway house and a drug treatment center.

Rubin graduated Phi Beta Kappa from Marshall College and received his M.D. from Yale. He interned in Boston and then returned to Yale for a residency in psychiatry from 1958 to 1961. He served two years as a captain and staff psychiatrist in the U.S. Air Force.

He then moved to Washington, joining the faculty at George Washington University as an assistant professor and working his way up to full clinical professor by 1977. He maintained a private practice and was a consultant to National Medical Enterprises after his involvement with Psychiatric Institutes of America. His research focused on forensic psychiatry and the relationships between law enforcement organizations and communities. He published *The Police and the Community* in 1972 and edited *Readings in Law and Psychiatry*.

JOHN C. WONG, M.D. '81, an orthopaedic and hand surgeon, died on November 6, 2000, in San Francisco. He was 44.

Wong had practiced as an orthopaedic and hand surgeon since 1987. He was a native of Hong Kong and was on the board of trustees of the Chinese Community Health Care Association.

JOSEPH F. ZIGARELLI, M.D. '40, a well-known neuropsychiatrist and Bronze Star Medal winner, died April 2 at Bethesda Memorial Hospital in Boynton Beach, Fla. He was 85.

Zigarelli graduated from Cornell University, then received his M.D. from Yale in 1940. He maintained a private practice in neuropsychiatry for over 50 years in Paterson and Morristown, N.J. He was chief of children's psychiatry at the state hospital of New Jersey at Greystone Park, and he was also on the staffs of Paterson General Hospital, Morristown Memorial Hospital and Columbia Presbyterian Hospital. His research and surgical techniques were directed toward finding alternatives to lobotomy, and were considered groundbreaking in their time.

He served in World War II and received the Bronze Star Medal for his heroic medical treatment of the citizens of Naples, Italy.

ALUMNI QUESTIONNAIRES TO BE MAILED SOON

The School of Medicine will publish an updated alumni directory in the autumn of 2002, providing contact and professional information for more than 11,000 graduates of the School of Medicine and its training programs. The directory will list alumni alphabetically and by program, class year, geographic location and area of medical specialty. The last medical school alumni directory was published in 1997.

The Bernard C. Harris Publishing Co. will be mailing a questionnaire to each alumnus and alumna during the next several months. Please complete the form and return it as soon as possible. If we don't have your current address, please contact the O ; ce of Alumni A=airs at the address below so we can make sure you receive a directory questionnaire.

Association of Yale Alumni in Medicine
Spinelli Office of Alumni Affairs
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P.O. Box 7613
New Haven, CT 06515
Phone: (203) 785-4674
Fax: (203) 737-5153
Website: info.med.yale.edu/ayam

FROM "AN AFRICAN SUMMER" BY ROBERT MCROBERTS, M.D. '66, IN THE WINTER 1966 ISSUE OF *YALE MEDICINE*: "Upon arriving in Ganta [Ganta Methodist Mission Hospital in the hills of eastern Liberia], I soon discovered that tropical medicine would be considered a general practice by American standards. For example, on any given morning the first five people in the clinic line might include a child with amoebic dysentery, a man suffering for a long time with onchocerciasis, a boy whose blood smear for *P. falciparum* is 6 plus positive, a pregnant mother of eight who complains of back pain, and an old man whose scrotum extends almost to his knees.

Later in the morning things might become somewhat more hectic. While you are examining a child with chickenpox, you send a man who has obviously broken his femur to the emergency room and hope that the woman who has just been taken into the examining room doesn't have an ectopic pregnancy as suspected. It's hectic because you can't send the man with the broken femur to X-ray. Instead you do the alternative: that is, you roll out the old U.S. Army field unit and trust that there'll be enough power to take a respectable film. You can't send the pregnant woman to surgery for, unlikely as it might seem, you are surgery! In many ways one might consider such an experience a rotating internship. But instead of rotating every two months, you rotate with each new patient."

FROM WINTER/SPRING 1981: "Growth in medicine has meant growth in the Library. ... A visit to the computer-search office gathers in a few minutes a volume of citations that would have taken days of hand searching. The computer terminal has available to it Medline, the online database equivalent to the last three years of Index Medicus. ... Technology now being developed holds even greater promise for libraries and library users. The National Library of Medicine, which developed Medline in the sixties, is working on a videodisk system that could fundamentally alter the concept of publishing. Electronic 'publication' of journals, whether through videodisks or some other method, would eliminate paper copies. Readers could use computerized bibliographic searching to find references, then scan the articles on a computer terminal screen. ...

Eventually, perhaps as soon as the end of this century, books too would be published in electronic form. While older books and journals would survive—and need to be stored—current publications would take up far less room. And their content would be available to computerized searching, freeing researchers from mechanical tasks to concentrate on the information itself."

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