

yale medicine

spring 2005

When molecule meets
computer chip


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Lessons from the depths

From color-tagged proteins
to transparent eggs and oversized
neurons, our water-dwelling
cousins are providing new tools
for scientists exploring
human disease
and physiology.



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Zebrafish, usually found swimming in rice paddies along the Ganges River, peer out from a tank in the laboratory of Zhaoxia Sun, one of two scientists at Yale who use the freshwater fish as a model organism.

BACKGROUND

Zebrafish grow quickly, progressing from egg to fish in a day. The eggs are transparent and develop outside the mother's body, allowing scientists to observe development as it occurs.

Photographs by Frank Poole

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



The 80-hour week, and its aftermath

I read with interest your recent article on resident hours ["Re-creating the Residency," Fall/Winter 2004]. I was among the physicians who testified at the grand jury that investigated the Libby Zion case. While it is true that the grand jury did not indict anyone, they did find that there was a significant cause for concern and issued a report to the New York state legislature. This led to the formation of the Bell Commission, which recommended the 80-hour work-week and increased supervision of house staff. It was this report that ultimately led to the passage of the 80-hour limit for house staff in New York.

The invective from organized medicine against these rules was ferocious. It put medicine at direct odds with the public, for whom these rules were self-evident and made unquestionable common sense. They believed that no one could work 100 to 120 hours a week and still provide the level of care and cognitive functioning that the public required of their physicians. They also intuitively understood that the more physicians were asked to deny their own needs while in training, the less they would be able to cater to the needs of their patients while

in practice. The more medicine railed against the rules, the more the public began to question its judgment. As you correctly pointed out, in many ways this was one of the strong impetuses for the patient safety movement. In addition, as medicine chose to specifically break the law in New York by not adhering to the hours limit, the public perceived medicine as viewing itself as being above the law, as being paternalistic and as acting in its own financial best interests. The resulting furor has led, in part, to the distrust that has been increasingly seen in the public's opinion of American medicine.

Yale has now taken a leading position in the intelligent implementation of these rules. Yale's leaders assessed the problems for patient care that the rules raised and put into effect specific solutions that addressed them. They committed themselves to an ongoing look at the process and continued improvement as problems arise. The resulting system of training will be good for patient care, house staff training and the view of medicine by the public.

Gerald M. Brody, M.D. '77
Tuckahoe, N.Y.

Enlightened HMOs make time for CME

Writer Jill Max quoted Lawrence S. Cohen, M.D., as saying: "One of the challenges in the environment is that physicians, because of managed care, find it increasingly difficult to leave the practice and go to a meeting." ["Yale CME Gets a New Lease on Lifelong Learning," Fall/Winter 2004.] I find this statement contrary to my experience with the Southern California Permanente Medical Group (SCPMG), a part of Kaiser-Permanente.

I joined SCPMG in July 1967 and became chief of ob/gyn. From the beginning, my department had weekly, mandatory, half-day CME meetings plus a weekly Friday morning hour for quality review. Speakers from the Department of Reproductive

Medicine at the University of California, San Diego, were often present. Later, when the UCSD residency began, our hospital was the first in San Diego to have a resident.

Our partnership agreement specifies a half-day weekly of paid education time plus one week paid yearly to attend an educational meeting. I never had these benefits when I was in solo practice in Brockton, Mass. Because of these educational opportunities, as regional clinical coordinator for SCPMG, I was involved in improving the quality of practice. Two of our hospitals, in San Diego and Los Angeles, became No. 1 and No. 2 in the state for quality.

Myron K. Nobile, M.D. '47, HS '54
La Jolla, Calif.

Dr. Cohen responds: "My comments did not apply to groups such as yours, but they do apply to the average practitioner who is in a solo or group practice. In that instance, time away at conferences that award CME credits are not easily come by. It is true that grand rounds and specialty conferences are often given at the hospitals, but many physicians are not encouraged to attend; I applaud the success of your program at Kaiser-Permanente."

HOW TO REACH US

Yale Medicine welcomes news and commentary. Please send letters to the editor (250 words or less) and news items to *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612, or via electronic mail to yymm@yale.edu, and include a daytime telephone number. Submissions may be edited for length, style and content.

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Merson steps down as dean of public health

As this issue of *Yale Medicine* was being prepared, we learned that Michael H. Merson, M.D., the Anna M.R. Lauder Professor of Public Health, would step down as dean of public health and chair of the Department of Epidemiology and Public Health (EPH), as of December 31, 2004. Brian P. Leaderer, M.P.H. '71, PH.D. '75, the Susan Dwight Bliss Professor of Public Health, was named interim dean and chair during a search for a successor to Merson. Nancy H. Ruddle, PH.D. '68, the John Rodman Paul Professor of Epidemiology and Public Health, will serve as interim deputy dean and vice chair.

Merson came to Yale in 1995 from the World Health Organization in Geneva, where he directed the Global Programme on AIDS. At Yale he continued his efforts to stem the pandemic, forming the Center for Interdisciplinary Research on AIDS (CIRA), which undertakes research and prevention programs in the United States, Russia, China, India and South Africa.

He has also raised the profile of the public health school and has fostered joint-degree programs with other professional schools at Yale, including nursing, law, management, forestry and environmental studies, and divinity.

After a sabbatical, Merson will return to the public health faculty later this year. He will also continue as director of CIRA.

Leaderer joined the EPH faculty in 1976 and is the principal investigator of studies that examine environmental and genetic factors of asthma in children. Ruddle directs graduate studies in public health. She studies cell trafficking and inflammation, particularly with regard to the lymphotoxin/tumor necrosis factor family. She has been on the Yale faculty since 1975.

yale medicine

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Fish tales, on the up and up

Last September, I was listening to a lecture in the Anlyan Center when a fascinating bit of data flashed on the screen. Assistant Professor of Genetics Zhaoxia Sun, PH.D. '98, was describing her use of zebrafish as a model organism for the study of polycystic kidney disease and alluded to how compact and convenient they are for laboratory work. The 600 small tanks on racks in her lab at the medical school can hold as many as 15,000 zebrafish, a species whose DNA bears a remarkable similarity to our own genetic code. Given the rapidity with which zebrafish develop (from egg to fish in a day), Sun has a powerful resource for conducting genetic studies relevant to human illness.

We wondered what other aquatic organisms were assisting scientists at the School of Medicine as they explore the dimensions of normal biology and disease. Sea hares, with their elongated neurons, and sea squid, with synapses so wide they can be seen without a microscope, are among the creatures writer Jennifer Kaylin encountered while reporting this issue's cover story ("Lessons From the Depths," page 18). She also learned how knowledge of chloride transport in dogfish sharks may one day help solve the riddle of cystic fibrosis and how a professor of physiology and neurobiology is exploring Australia's Great Barrier Reef to discover and clone new fluorescent proteins from coral. These molecules may prove useful for tagging cells and exposing what happens inside them—in real time and brilliant color.

Science and medicine are always changing, and it's gratifying to know that Yale faculty are leading the way in areas such as these, asking the questions that open doors to new knowledge. That curiosity and sense of adventure can only benefit doctors and patients around the world—and across the seven seas—for years to come.

Michael Fitzsosa

SECOND OPINION BY SIDNEY HARRIS



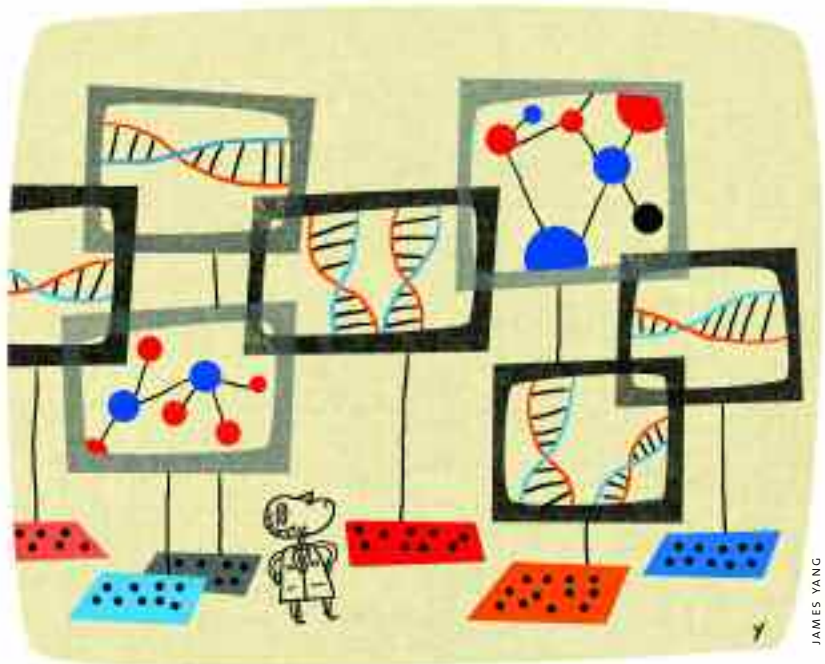
The molecule meets the computer chip

Harnessing the power of computers is essential as biologists work to decipher mountains of new data.

It is difficult to imagine two places more different than The Eagle Pub and Celera Genomics, each of which provided the setting for signal events in modern biology. The cozy Eagle, in Cambridge, England, was already a smoky anachronism fitted with burnished brass and dark wood in February 1953, when Francis H.C. Crick famously burst through the door to inform James D. Watson that they had jointly deciphered “the secret of life”—the structure of DNA. Nearly 50 years later, in Celera’s sterile, starkly lit “sequencing rooms,” and in similar rooms at institutions responsible for the government-sponsored Human Genome Project, the complete human genome was painstakingly unraveled by row upon row of humming computers.

The pub and the sequencing room are apt metaphors for the vast changes wrought by Watson and Crick’s discovery, which unleashed a torrent of research in molecular biology that has revolutionized our understanding of evolution, physiology and disease. Watson and Crick confronted a blank slate, but today’s scientists are awash in a fast-moving river of information so thick with possibility that the American Association for the Advancement of Science recently felt compelled to sponsor a symposium for biologists called “Inundated With Data.”

The collective efforts of the world’s scientists have allowed us to construct



JAMES YANG

diagrams of intracellular signaling pathways that would make a New York subway official blanch, and the complete genomes of over 100 organisms are now in hand. However, biologists have been so busy amassing fine details that they have had little time or incentive to step back from the bench, take a breath and begin to grasp the essential patterns in the big picture.

Luckily, computing power has increased in tandem with biological knowledge at an exponential rate, setting the stage for the recent emergence of the cutting-edge, multidisciplinary field of computational biology. The field embraces genomics and proteomics (the latter aims to catalog the complete inventory of proteins encoded by genomes), but also promotes computational modeling of intracellular processes and cell-cell interactions, as well as the “high-throughput” data-mining techniques of

bioinformatics, which can unveil common mechanisms underlying seemingly diverse diseases and compare genomes to discern subtle evolutionary relationships among organisms.

In 2003, Yale established an interdisciplinary PH.D. program in computational biology and bioinformatics. That same year, the university’s Biological Sciences Advisory Committee (BSAC), under the leadership of H. Kim Bottomly, PH.D., professor of immunobiology, began a study which concluded that computational approaches would play a central role in 21st-century biology. The committee has just produced its final report, a blueprint for Yale to stay ahead of the curve in faculty recruitment, funding and facilities.

The committee’s efforts also led to “A Look to the Future,” an October symposium at the medical school’s Anlyan Center chaired by Perry L. Miller, M.D.,

PH.D., professor of anesthesiology and director of the Center for Medical Informatics; Mark B. Gerstein, PH.D., the Albert L. Williams Associate Professor of Biomedical Informatics and associate professor of molecular biophysics and biochemistry; and William L. Jorgensen, PH.D., the Conkey P. Whitehead Professor of Chemistry.

The symposium assembled seven top researchers from around the world who use computational approaches to attack a variety of biological problems, from untangling phylogenetic relationships between species to manipulating gene sequences to create completely new proteins and enzymes with customized biological functions.

In addition to providing a forum for these scientists to present their latest work, the symposium also included several informal brainstorming sessions where Yale scientists and administrators learned how the speakers' home institutions have risen to the structural and organizational challenges of integrating computational biology into teaching and research.

The BSAC report argues that Yale must increase its research and teaching strengths in computational biology and bioinformatics. It recommends the creation of thematically oriented clusters of faculty at the medical school and on Science Hill. And it proposes the formation of a universitywide center for computational biology and bioinformatics that would foster campuswide interactions of faculty and trainees and provide administrative support.

No one doubts that computational biology is here to stay. "The old view was that biologists were the scientists who didn't like to think quantitatively," said Carolyn W. Slayman, PH.D., Sterling Professor of Genetics and deputy dean for academic and scientific affairs. "Now, biologists must face up to the fact that there's going to be a demand for greater computational skill and greater expertise in informatics than ever before—it's the future of the field."

—Peter Farley

A new hospital pavilion, set to open in 2008, will house \$430 million cancer facility

Services for cancer patients are currently scattered at six sites across the Yale-New Haven Medical Center, but that will change by 2008 with the planned opening of a new hospital facility that will offer all cancer services under one roof and significantly enhance the medical school's ability to conduct clinical research.

At a press conference on November 30, Yale-New Haven Hospital (YNHH) President and CEO Joseph A. Zaccagnino, M.P.H. '70, announced that YNHH would add a 497,000-square-foot north pavilion to the YNHH complex that will house a comprehensive clinical cancer center. The plan will add 112 inpatient hospital beds and an estimated 400 permanent jobs.

The proposed \$430 million center is a 14-story facility with space for operating rooms; infusion suites; radiation treatment rooms; adult inpatient facilities for surgical, medical and gynecologic oncology; and an outpatient women's cancer center. It will be connected to the Yale-New Haven Children's Hospital by way of a five-story bridge across the upper floors, so that pediatric patients will be able to receive treatment at the new center while remaining hospitalized in the children's facility.

"I cannot overstate our level of enthusiasm and excitement about this project," Dean Robert J. Alpern, M.D., said at the press conference, attended by city officials, patients, employees and community, hospital and medical school leaders. "Now that we've seen

the drawings, we're impatiently ready to move into the building. We're going to have to control ourselves." Yale Cancer Center Director Richard Edelson, M.D. '70, called the move "a huge step forward."

Alpern and Yale President Richard C. Levin both stressed the opportunities the new center opens up for conducting additional clinical trials, which are a source of promising new treatments for patients and an important revenue stream for academic medical centers. Levin noted that Yale is already one of the top biomedical research institutions in the world and does excellent cancer research in the laboratory.

"With expanded capabilities to treat cancer patients and to do research on the efficacy of new therapies, we can do much more," Levin said. "We can establish ourselves as one of the world's great centers for the treatment of cancer."

The new center will be built on existing hospital property at the site of the Grace Building on Park Street, a former nursing hall now given over to offices, which is slated for demolition this spring. The hospital's board of trustees approved plans for the center in November, following state approval of the preliminary site plan last July. Pending approval of the plans by the city and state, groundbreaking is expected in the fall.

—Michael Fitzsosa



An artist's rendering shows a new pavilion at Yale-New Haven Hospital, which will house all cancer services under one roof. It is expected to open by 2008.

New MBA program to help health professions with the business of medicine

At some point in the 1980s, according to Howard P. Forman, M.D., M.B.A., vice chair and associate professor of diagnostic radiology, the practice of medicine became more pain than gain for many physicians.

“Health care costs were skyrocketing and cost containment measures gained importance,” said Forman. “Physicians were targeted as the cause of the problems and were counted on to bring down costs.”

Forman and others at Yale’s schools of medicine, management and public health may have a prescription for this malaise—the Yale MBA for Executives: Leadership in Healthcare. This new program, which Forman co-directs with Stanley J. Garstka, Ph.D., deputy dean of the School of Management, and Dick R. Wittink, Ph.D., the George Rogers Clark Professor of Management and Marketing, will enroll a charter class of up to 30 students in August.

The 22-month program’s goals—besides providing a second set of skills without career disruption—are to turn the classroom into a cross section of the contemporary health care field and to train what Forman calls “change agents capable of making a positive difference in the practice of health care.” By enrolling students with a broad range of background and experience—professionals from hospitals, clinics, insurance and managed-care organizations and pharmaceutical, biotechnology and financial service firms—the program aims to change perceptions that these fields are adversaries. Then, through two intense residences, weekend classes and seminars with visiting scholars, the curriculum provides the management skills needed to navigate the complexities of health care, which is itself constantly changing due to medical and technological breakthroughs, new laws and government policies.

The seed for the executive program was planted in 1996 when medical students expressed interest in an M.D./M.B.A. program. That joint-degree program, though geared toward medical students, has also attracted faculty and working physicians. Among the latter, Michael Apkon, M.D., Ph.D., FW ’94, M.B.A. ’02, was one of the four M.D./M.B.A.s produced by the first graduating class in 2002. A former assistant professor in the medical school, he is now medical director of the pediatric ICU and a vice president at the Yale-New Haven Children’s Hospital.

Although that program worked for medical students, who could add a year to their studies, it was not ideal for practicing professionals. “Surgeons came to me and said, ‘I’d have to give up my career if I’m going to do this joint-degree program because I can’t do four days a week and not be in the OR.’ So we started work on an executive program targeted to health care professionals,” said Forman.

Not so long ago, even the idea of an M.D./M.B.A. was a tough sell. “There was the fear that you were either selling out to the enemy or selling your soul,” said Forman. That negative perception was changed, in part, by the University of Pennsylvania’s Wharton School, where William L. Kissick, M.D. ’57, M.P.H. ’59, DR.PH. ’61, led an M.D./M.B.A. program that produced some of today’s health care leaders (See *Alumni Faces*, p. 38).

“By the 1990s, it was apparent that for those who want to be leaders this is an appropriate path—that you’re not selling out,” said Forman. “You’re fulfilling your mission to improve health care for larger numbers than you could as a pure clinician.”

—Alan Bisbort

Yale and New Haven join in pilot program for treating HIV/AIDS in Russia

Russia today is where the United States was 20 years ago in dealing with HIV/AIDS: denial and prejudice are almost as widespread as the disease itself.

In an effort to help, last July in St. Petersburg Health and Human Services Secretary Tommy G. Thompson announced a major grant to fight the AIDS epidemic. A Yale doctor and epidemiologist were by his side, and at an October news conference in New Haven’s City Hall, they announced their own role in the initiative. The School of Medicine was one of four U.S. organizations chosen to receive \$320,000 each from the U.S. Agency for International Development to provide training in care, treatment and support services to people living with HIV/AIDS in Russia.

The School of Public Health, through its Center for Interdisciplinary Research on AIDS, has worked on training and prevention programs with colleagues in St. Petersburg since 1998. But this marks the first collaboration between the two cities to address HIV/AIDS care and treatment.

The 30-month program calls for Yale, along with state and city agencies, to share information and strategies with colleagues in St. Petersburg. The grant will fund four exchanges each year; the first group of Russian trainees arrived in New Haven in early October. Yale faculty and representatives from community-based HIV/AIDS organizations will also travel to St. Petersburg to train Russian health professionals and to observe how they are managing the epidemic.

In Russia, a major obstacle is the prejudice against HIV/AIDS patients, typically young, male intravenous drug users. As part of the program, Russian visitors will observe services provided by the Yale AIDS Program and organizations in New Haven, and they will visit a methadone clinic and needle

exchange program. Krystn R. Wagner, PH.D. '89, M.D. '96, assistant professor of medicine and project coordinator of the New Haven–St. Petersburg partnership, said she hopes that “observing drug treatment here will help catalyze new thinking about substance abuse management and the care of drug users.”

The problem in Russia, said Robert Heimer, PH.D. '88, associate professor of epidemiology and public health and co-coordinator of the project, is the lack of a multidisciplinary, integrated system for managing HIV/AIDS. “Someone walks into a hospital and is treated for HIV,” said Heimer, “but what about his drug addiction, or the fact that he has tuberculosis or that he’s homeless? There’s no coordination, no system that allows them to deal with the complexities of this illness in a way that crosses traditional medical boundaries.”

The impetus for this initiative is the soaring number of HIV infections in

Russia. HIV/AIDS didn’t surface in the countries of the former Soviet Union until the early 1990s, but they now report some of the world’s fastest-growing rates of new infections. Although there are 300,000 reported cases in Russia, the United Nations and Russian AIDS officials put the number at 1 million or more. Wagner, medical director of the Nathan Smith Clinic, the HIV clinic affiliated with Yale-New Haven Hospital, said this is due to many factors, including relaxed border controls after the dissolution of the Soviet Union, rising unemployment and drug trafficking. Most new HIV cases were initially among IV drug users, but now cases caused by sexual transmission are on the rise.

Heimer called the collaboration “remarkably exciting. ... If we can create and implement an integrated system on a pilot basis in one small region of St. Petersburg, and if it’s successful, it can be replicated elsewhere in Russia.”

—Jennifer Kaylin



JOHN CURTIS

Health officials in the 300-year-old city of St. Petersburg have joined with New Haven and Yale in a new effort to coordinate medical and social services for people infected with HIV/AIDS. The epidemic in Russia, originally prevalent in drug users, is poised to spread through sexual transmission.

et cetera ...

KAPLAN NAMED TO IOM

Edward H. Kaplan, PH.D., the William N. and Marie A. Beach Professor of Management Sciences at the School of Management and professor of public health, has been elected to the Institute of Medicine. Kaplan, the only Yale faculty member named to the institute this year (see *Alumni* on page 42 for more on this topic), is an operations research and statistics expert who studies problems in public policy and management. His recent research has focused on counterterrorism topics such as the tactical prevention of suicide bombings, bioterror preparedness and response logistics in the event of a smallpox or anthrax attack. In the early 1990s, he was the principal investigator of a landmark project that evaluated the efficacy of New Haven’s needle exchange program.

Membership, one of the highest honors in medicine, is awarded for contributions to medical science, health care and public health. The institute was established in 1970 by the National Academy of Sciences and provides independent, scientifically informed analysis and recommendations on human health issues.

—John Curtis

YALE JOINS NATIONAL EPILEPSY STUDY

Yale has been named a key member of a national group of medical centers that has received the largest grant ever for a study of epilepsy in children. The \$17 million award from the National Institute of Neurological Disorders and Stroke will fund a study of the three most-used drugs for treating childhood absence (petit mal) epilepsy. The five-year study at 20 sites across the country will attempt to determine the best initial medicine for childhood absence epilepsy, which involves seizures marked by nonconvulsive staring spells.

At Yale researchers will try to identify why some treatments work, why some have side effects and what effects they have on cognition, behavior and learning. “This is the first step toward our goal of making it possible for physicians to predict patient response and tailor therapies for individual needs,” said Edward J. Novotny Jr., M.D., FW '89, who is leading the study with colleague Susan R. Levy, M.D.

—J.C.



EINAT PELED

Minority patients wait longer for angioplasty

Researchers say the choice of hospital is a bigger factor than differential treatment in the hospital.

Minority patients with heart attack symptoms wait longer for treatment than whites do, according to a recent study led by Harlan M. Krumholz, M.D., M.Sc., professor of medicine (cardiology), and Elizabeth H. Bradley, Ph.D. '96, associate professor of public health (health policy and administration). But waiting time appears to have more to do with the choice of hospital than any conscious decision by health care providers to discriminate based on race or ethnicity.

For the study, published in the October 6 issue of *JAMA: The Journal of the American Medical Association*, researchers examined data from the National Registry of Myocardial Infarction (NRFMI) to determine how much time elapsed between a patient's arrival at the hospital and the start of either drug therapy or balloon angioplasty. Records of more than 110,000 heart attack patients treated between January 1999 and December 2002 were analyzed.

At first glance, the results showed that door-to-drug times for minority patients were significantly longer—up to seven minutes for African-Americans—than for white patients, while door-to-balloon times for this group were almost 19 minutes longer. However, once the study factored in the hospitals that were offering treatment, these differences were substantially reduced: it took about five

minutes more for African-Americans to receive drugs and nine minutes more for balloon intervention. For other ethnic groups, the differences were reduced even further.

"People who get care quicker when they are having a heart attack are more likely to live, so this is an important difference to understand and address," said Bradley. "The biggest insight from this paper was that it seems as if there were two levels of difference going on," said Krumholz. "There's the level where race/ethnicity differences exist, and although they're small, they're disturbing and need to be understood. But a bigger part of the overall difference in treatment by race and ethnicity seems to be explained by the hospitals that people are going to."

Previously, researchers assumed that racial and ethnic disparities were due to differential treatment inside the hospital, without considering the possibility that hospitals that treat greater numbers of minority patients do not offer the same level of care as hospitals that treat fewer minority patients. "Our finding suggests that the issue is bigger than differential treatment inside the hospital. Minority patients tend to be treated at hospitals with poorer quality in this area generally," Bradley said.

The study suggests that efforts focusing solely on racial and ethnic disparities will fall short in improving patient care. Hospitals need to examine how they're delivering care and formulate systems that address inadequacies. "As one solution, we should really identify the characteristics and key processes that raise the quality of hospitals generally and ensure that we target these kinds of improvement efforts in hospitals that have poorer quality indicators, many of which are hospitals where minorities receive their care," Bradley said.

—Jill Max

et cetera ...

Camera in a pill gives an unprecedented view of the small intestine

When the White Queen assured Alice in Wonderland that she was able to believe “as many as six impossible things before breakfast,” the idea of swallowing a tiny camera first thing in the morning was probably not on her list.

But thanks to a new procedure called video capsule endoscopy, some patients with gastroenterological symptoms are doing just that. The camera, enclosed in a pill about the size of a large vitamin supplement, is swallowed early in the morning on an empty stomach; the patient drinks water two hours later and eats a light lunch two hours after that to encourage the gastric and intestinal contractions that move the video capsule along. During its eight-hour passage through the digestive tract, the camera transmits images of the small intestine to a monitoring device around the patient’s waist. The resulting pictures, downloaded into a computer, allow the clinician to see parts of the small intestine that are not visible through a regular endoscope.

According to Deborah D. Proctor, M.D., associate professor of medicine (digestive diseases), who has been using the technique since it was introduced at Yale last spring, it is helpful in diagnosing hidden gastrointestinal bleeding where upper endoscopy and colonoscopy are inconclusive. It is also useful in obtaining information about management of chronic problems such as Crohn’s disease, which depends on the degree to which the disease is located in the small intestine.

“Upper endoscopy shows only about a foot of small intestine,” Proctor noted. “The enteroscope shows only about another 6 to 8 feet—a total of about one-third to one-half of the small intestine. With the camera we can see the entire small intestine in about 85 percent of patients who undergo the procedure.”

Scanning technology—using a camera at the end of a scope to transmit data, as is done with an endoscope—has been around for about 15 years, while fiber optic technology has been around for about 30 years. What is new here is the camera-inside-the-pill—a technique that originated in Israel four years ago and is currently in use at Yale and 250 other facilities around the country.

“The procedure is totally noninvasive; no radiation is involved, there is no discomfort and no need for sedation,” she said. “Once the camera and belt are in place, patients can go about their normal day.”

The only contraindication is for those patients whose GI tracts might be obstructed, preventing the capsule from moving through. For all others the capsule moves painlessly through the GI tract and is excreted.

“This is so safe that we’ve started using it with children—as long as they weigh over about 50 pounds,” Proctor said. “Being able, for instance, to see active bleeding and know exactly where it is coming from has great potential to improve GI disease diagnosis and management.”

—Rhea Hirshman

MELANIN CAN BE GOOD, OR BAD

It’s common knowledge that blondes and redheads need more protection from the sun to prevent skin cancer, but a Yale scientist may have discovered why. The culprit may be the melanin in the follicles of light-colored skin, Douglas E. Brash, PH.D., professor of therapeutic radiology and genetics, reported in a study published in the *Proceedings of the National Academy of Sciences* in October.

Brash began his research to determine why fair-skinned but dark-haired people were less vulnerable to skin cancer than blondes or redheads. He found that among the fair-haired, melanin, the source of skin and hair color which usually protects the skin from ultraviolet (UV) rays, actually magnifies the rays’ damaging effects. For the study, he irradiated mice of various hair colors with UV rays and found pronounced cell death in yellow-haired mice.

“What this tells us is that melanin is not just good for you, it can also be bad,” Brash said. “It depends on the color of your particular melanin.”

—John Curtis

GAMBLING AND ELDER HEALTH

A study by Yale researchers published in *The American Journal of Psychiatry* in September has found a link between good health and gambling among the elderly. Younger gamblers, however, show high rates of alcohol use and abuse, substance abuse, depression, incarceration and bankruptcy.

In a telephone survey of 2,417 adults, gamblers 65 and older were far more likely to describe their health as excellent or good, but the researchers haven’t determined why. One theory is that better health enables older people to take part in activities including gambling.

“Although the underlying reasons remain hypothetical, proposed reasons included the increased activity, socialization and cognitive stimulation that are related to engaging in gambling,” said Rani Desai, M.P.H. ’91, PH.D. ’94, associate professor of psychiatry and public health and one of the authors of the report. “Such a mechanism would be consistent with the literature on healthy aging, which indicates that more socially and cognitively active elders are, in general, healthier.”

—J.C.

A new role for “good” microorganisms

Findings at Yale question the consensus on how the immune system interacts with bacteria.

The human immune system is a finely honed defense mechanism that quickly detects and destroys bacterial and viral invaders. But so-called “good” bacteria—which perform useful physiological roles—are a puzzling exception: they somehow slip under the immunological radar and form flourishing colonies on or in our bodies. Such “commensal microflora” are particularly abundant in the colon, which teems with some 10 trillion bacteria that help to metabolize nutrients and guide normal tissue development.

The scientific consensus has been that the immune system overlooks the colon’s commensal microbes because they remain “sequestered” within a layer of epithelial cells. However, the immune system does sometimes attack the colon’s commensal bacteria, causing inflammatory bowel diseases such as Crohn’s disease and ulcerative colitis.

In 1997, in collaboration with the late Charles A. Janeway Jr., M.D., Ruslan M. Medzhitov, PH.D., professor of immunobiology, discovered *toll*-like receptors (TLRs), a new class of molecules in the innate immune system [“The *Toll* Road,” Spring 2002], and he suspected that they might be involved in inflammatory bowel diseases. To find out, he and his colleagues injected DSS, a substance that kills colonic epithelial cells, into both normal mice and mice with non-functional TLRs. Because of the TLRs’

assumed role in inflammatory bowel diseases as attackers of good bacteria, the researchers fully expected that there would be no inflammation in the mice with the disabled TLRs.

But to Medzhitov’s amazement, the opposite occurred. As reported last July in the journal *Cell*, even the smallest doses of DSS had no effect on normal mice, but in the mice with compromised TLRs they caused marked weight loss, severe colonic bleeding and death. Moreover, tissue samples from the colons of these mice showed that the normal cell cycle was profoundly disrupted. In short, TLRs looked more like defenders than attackers.

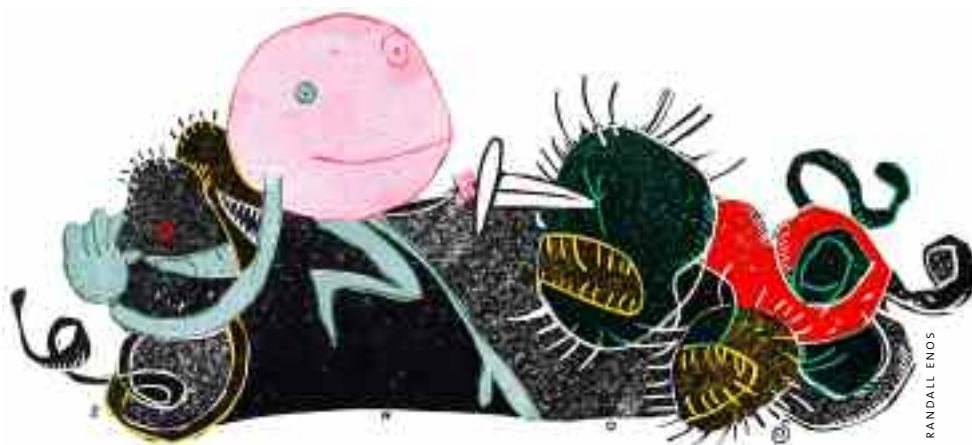
These startling findings led Medzhitov to question the long-held view that commensal microbes are fully shielded from the immune system. Instead he surmised that commensal bacteria may be only partially sequestered, and that recognition of these bacteria by TLRs triggers the production of molecules that protect the colon. In the case of acute epithelial injury, a TLR response to exposed microflora might efficiently recruit and direct healing molecules.

To test these wholly new ideas, Medzhitov and his colleagues turned their original procedure on its head. Instead of knocking out TLRs genetically, they used antibiotics to eliminate good bacteria from mice with normal TLR activity. Doses of DSS caused the same profuse intestinal bleeding and high mortality rate found in mice with faulty TLRs. But DSS caused no ill effects in mice that had received bacterial fragments known to activate TLRs.

“Because this all was so unexpected, it brought up a lot of questions that we’re following up now and finding a lot of interesting and surprising results,” said Medzhitov. But he believes that the studies have one immediate implication for clinical practice. Patients at risk for opportunistic infections, including those undergoing treatment with radiation or chemotherapy, routinely receive powerful antibiotics that kill off commensal intestinal flora. By combining antibiotics with TLR-activating compounds such as the bacterial fragments used in his mouse studies, Medzhitov says, it may be possible to prevent infection while triggering tissue protective responses needed to repair damage induced by radiation and chemotherapy.

“This idea could be directly relevant, and could be tested in clinical trials and used in patients—if not the precise regimen, the basic approach,” Medzhitov said. “That would be very exciting.”

—Peter Farley



Lipid found to play key role in transmitting information between synapses

Yale researchers have found that a membrane lipid plays a crucial role in communicating information between synapses in the brain, according to a study published in *Nature* in September.

“This study is the first to show that lowering the levels of this lipid in nerve terminals affects the efficiency of neurotransmission,” said senior author Pietro De Camilli, M.D., FW ’79, the Eugene Higgins Professor of Cell Biology and a Howard Hughes Medical Institute investigator.

De Camilli and his team started by genetically engineering laboratory mice that lacked an enzyme, PI3K1-gamma, which in turn plays a role in synthesizing the lipid under investigation, phosphatidylinositol-4,5-bisphosphate—or PtdIns(4,5)P₂—a member of a class of lipids called phosphoinositides. The mice born without PI3K1-gamma were apparently normal, but they were unable to feed and died quickly. Studies of their nervous systems revealed lower levels of PtdIns(4,5)P₂ and a partial impairment both of the process of fusion of synaptic vesicles and of their recycling.

De Camilli’s laboratory has studied extensively the mechanism underlying cycling of synaptic vesicles, small sacs that contain neurotransmitters that exchange information between neurons. Synaptic vesicles release their contents at junctions between nerve terminals by fusing with the plasma membrane, where they rapidly reinternalize, reload with neurotransmitter and are reused.

These studies not only provide new insight into basic mechanisms in synaptic transmission, said De Camilli, a member of the Kavli Institute for Neuroscience at Yale, but also have implications for medicine. For example, Down syndrome patients have an extra copy of the gene encoding the enzyme synaptojanin 1, which degrades PtdIns(4,5)P₂ in the brain. Patients with Lowe syndrome, who also have mental retardation, lack another PtdIns(4,5)P₂-degrading enzyme. Cancer and diabetes also can result from abnormal metabolism of phosphoinositides, De Camilli said.

“Typically, studies of synaptic transmission have focused on membrane proteins,” he said. “Only recently has the importance of the chemistry of membrane lipids and of their metabolism started to be fully appreciated. The field is still in its infancy, but rapid advancements in the methodology for the analysis of lipids promise major progress in the field and the possibility of identifying new targets for therapeutic interventions in human diseases.”

—Jacqueline Weaver

et cetera ...

ALZHEIMER’S PROTEIN SOLVED

Using X-ray crystallography, Yale scientists have discerned, for the first time, the atomic structure of a protein that is linked to Alzheimer’s disease.

Ya Ha, PH.D., assistant professor of pharmacology, reported in August in *Molecular Cell* that he had observed an unusual feature of human amyloid precursor protein (APP). Rare mutations of APP cause Alzheimer’s at an early age in a small number of people. Researchers have been trying to determine what APP does and how it converts to a smaller protein, amyloid beta-peptide, which forms neuronal and vascular amyloid deposits typical of Alzheimer’s disease.

Ha and Yongcheng Wang, PH.D., a post-doc in his laboratory, found that APP consists of two long rodlike molecules that form a tight complex, with the head of one molecule touching the tail of the other.

“That observation suggested a novel possibility,” said Ha, “that APP may function to mediate cell-to-cell contact by interacting with itself.”

—John Curtis

GROWTH FACTOR LINKED TO ASTHMA

Yale scientists have found that a molecule normally associated with the growth of new blood vessels in the lungs probably plays a role in asthma, raising the possibility of developing drugs that block the molecule’s receptors and signaling pathways.

The molecule, vascular endothelial growth factor (VEGF), induced asthmalike abnormalities when it was expressed in the lungs of transgenic mice, according to a report published in the journal *Nature Medicine* in September.

“To our surprise, in addition to growing new blood vessels, many features of asthma were also seen in these mice,” said principal investigator Jack A. Elias, M.D., the Waldemar Von Zedtwitz Professor of Medicine. “We saw mucus formation, airway fibrosis and asthmalike pulmonary function abnormalities. We also found that if you block VEGF, you block the asthmalike manifestations in other mouse asthma models.”

Elias and his team are currently examining how VEGF works at the cellular and molecular levels.

—Karen Peart

Flashcards for the boards

How two frustrated students decided to make studying for the Step 1 exam easier.



The project began after a bridge game in mid-January 2003, when two medical students were commiserating about preparing for the board exam. Bridge partners Suzanne J. Baron and Christoph I. Lee were frustrated by studying for Step 1

of the United States Medical Licensing Examination—no single source seemed to provide the information they needed about pathology.

To assemble the basic facts about more than 300 diseases covered in the pathology section of the exam, the two second-year students leafed through a half-dozen review books and textbooks. Somebody ought to make the job easier, they reasoned. And so, although they don't bet on their bridge games, Baron and Lee decided to gamble: they would develop a study aid, a set of flashcards, and they would sell it to a publisher.

Their efforts paid off. McGraw-Hill liked the idea, and three months after *Lange FlashCards: Pathology* came on the market last summer, more than 3,000 sets had sold. McGraw-Hill may translate the cards into Chinese, Greek, Italian, Spanish and Turkish for students in international medical schools who will take the Step 1 before applying for residencies in the United States.

Ironically, preparing the manuscript meant even more of the hard work that Baron and Lee had complained about. "I have a stack of review books this high in my apartment," says Baron with a laugh, holding her hand waist high.

The flashcards cover disorders in 13 systems in the human body, from the heart to the immune system. To put



JOHN CURTIS

Christoph Lee and Suzanne Baron delayed their clinical clerkships in order to develop a set of flashcards to help medical students prepare for Step 1 of the Medical Licensing Exam. The cards are now being marketed by McGraw-Hill.

the facts in context, Lee and Baron wrote a clinical vignette for the front of each card, and facts about the disease on the back. As Lee and Baron worked, they realized that students would find the cards useful not only in preparing for the boards, but also for studying pathology when it was taught in class. Two of their professors, John H. Sinard, M.D., Ph.D., HS '93, FW '94, associate professor of pathology and ophthalmology, and Deborah Dillon, M.D. '92, associate research scientist in pathology (now at Harvard), checked their manuscript for accuracy.

To find time for the project, Lee and Baron asked Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93, associate dean for student affairs, for permission to postpone their clinical clerkships, which their classmates began in June 2003. Angoff agreed that the project was consistent with the philosophy of the Yale System. "Students are encouraged to find the things they're passionate about and explore them in depth," she said. "I love the fact that they saw a need and they were going to be the ones to fill it." (This was not the first effort by Yale students or residents to prepare a study guide. Tao Le, M.D., HS '03, co-wrote *First Aid for the USMLE Step 1* while a Yale resident, with the help of students Antony Chu, M.D. '02, and Esther Choo, M.D. '01, who worked on the 1999 edition of the study guide.)

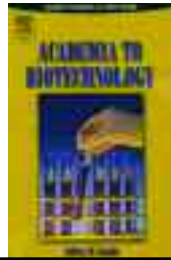
"We owe a lot to the Yale System," says Lee. Still, when they saw their friends begin work in the hospital, Baron recalls, "we felt a little left behind."

They have something to show for their time: a stack of 286 four-by-six flashcards, which retail for \$29.99. (The authors receive royalties of 10 percent.) As they apply for residencies in internal medicine (Baron) and diagnostic radiology (Lee), they're also working on flashcards for pharmacology and for biochemistry and genetics.

Recently, Baron spotted the cards on a shelf at the Barnes & Noble bookstore near her home in suburban Boston. "I said, 'That's me!' That was a huge thrill."

—Cathy Shufro

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



The Optimist: Meditations on Medicine

by Howard M. Spiro, M.D., professor emeritus of medicine (*Science & Medicine*) This compilation of essays by Spiro, which have appeared regularly in the pages of *Science & Medicine* since 1994, ranges broadly in subject from patients to technology to the state of medicine. Spiro addresses some recurrent themes: the importance of listening to the patient, consolation of the patient and the role of the physician as mediator between technology and patient.

A Doctor's Visit: Three Novellas & Five Short Stories

by Siegfried J. Kra, M.D., associate clinical professor of medicine (Lorenzo Press) These fictionalized stories, based on the author's personal history and experiences, explore the emotional lives of doctors and their patients and bring the realities of the medical profession to life.

Clinical Nuclear Cardiology: State of the Art and Future Directions, 3rd ed.

by Barry L. Zaret, M.D., the Robert W. Berliner Professor of Medicine, and George Beller, M.D. (Mosby) This book describes the most recent developments in technology, instrumentation and radiopharmaceuticals used in nuclear cardiology applications.

Invisible Cities: A Metaphorical Complex Adaptive System

by Chloé E. Atreya, PH.D. '04, M.D. candidate (Festina Lente Press) This work of creative non-fiction explores the principles of complex adaptive systems to demonstrate how art and science inform each other.

Academia to Biotechnology: Career Changes at Any Stage

by Jeffrey M. Gimble, M.D. '82 (Elsevier Academic Press) This book evaluates the abstract and practical aspects of moving from a university laboratory to a position in the biotech industry. It shows the parallels and contrasts between a postdoctoral fellowship and a job at a biotechnology company, and it provides "how-to" guides for the preparation of manuscripts, patents and grants.

Viral Encephalitis in Humans

by John Booss, M.D., FW '71, professor of neurology and laboratory medicine, and Margaret M. Esiri (ASM Press) The authors provide guidelines for diagnosing and treating viral encephalitis. Their recommendations reflect advances in molecular virology, imaging technology and molecular pharmacology.

Acid Related Diseases: Biology and Treatment, 2nd ed.

by Irvin M. Modlin, M.D., professor of surgery (gastroenterology), and George Sachs, D.Sc. (Lippincott Williams & Wilkins) This textbook explores the history, biology and treatment of acid-related diseases, including gastric and duodenal ulcer disease, gastroesophageal reflux disease, and the role of *H. pylori*.

Principles and Practice of Radiation Oncology, 4th ed.

by Carlos A. Perez, M.D., Luther W. Brady, M.D., Edward C. Halperin, M.D. '79, and Rupert K. Schmidt-Ullrich, M.D. (Lippincott Williams & Wilkins) This text is designed to provide a better understanding of the natural history of cancer, the physical methods of radiation application, the effects of irradiation on normal tissues and the most judicious ways in which radiation therapy can be used to treat cancer patients.

From Neuroscience to Neurology: Neuroscience, Molecular Medicine, and the Therapeutic Transformation of Neurology

by Stephen G. Waxman, PH.D., M.D., professor and chair of neurology, pharmacology and neurobiology (Elsevier Academic Press) Containing chapters by more than 29 internationally recognized authorities, this book reviews the development of new therapies in neurology from their inception in the laboratory to their introduction into the clinical world. It also explores evolving themes and new technologies that offer hope for even more effective treatments and, ultimately, cures for currently untreatable disorders of the brain and spinal cord.

A Woman's Guide to Menopause & Perimenopause

by Mary Jane Minkin, M.D. '75, HS '79, clinical professor of obstetrics, gynecology and reproductive sciences, and Carol V. Wright, PH.D. (Yale University Press) Drawing on new information from recent research, this book offers advice for women dealing with physical and emotional health issues surrounding menopause. Topics include the pros and cons of hormone replacement therapy; controlling the symptoms of PMS; and treatments for menopause-related hot flashes, insomnia and depression.

Cut Your Cholesterol: Featuring the Exclusive Live It Down Plan

by David L. Katz, M.D., M.P.H. '93, associate clinical professor of public health and medicine, and Debra L. Gordon (Reader's Digest Association) With advice about nutrition, physical activity, supplements and stress-management techniques, this book provides a plan to reduce cholesterol and lower blood pressure.

Cancer: Principles & Practice of Oncology, 7th ed.

by Vincent T. DeVita Jr., M.D., HS '66, the Amy and Joseph Perella Professor of Medicine, Samuel Hellman, M.D., HS '62, and Steven A. Rosenberg, M.D., PH.D. (Lippincott Williams & Wilkins) Acclaimed as "the ultimate authority on cancer," this volume reflects the latest breakthroughs in molecular biology, cancer prevention and multimodality treatment of every cancer type.



Healthcare for Children on the Autism Spectrum: A Guide to Medical, Nutritional, and Behavioral Issues

by Fred R. Volkmar, M.D., the Irving B. Harris Professor of Child Psychiatry, Psychology and Pediatrics in the Child Study Center, and Lisa A. Wiesner, M.D., HS '82, FW '83, assistant clinical professor of pediatrics (Woodbine House) This book offers parents of children with autism spectrum disorder information on issues such as sleep problems, unusual eating habits and impulsive or aggressive behaviors.

Locating Medical History: The Stories and Their Meanings edited by Frank Huisman and John Harley Warner, Ph.D., professor and chair of the Section of the History of Medicine (Johns Hopkins University Press) At a time when the study of medical history is facing choices about its future, these scholars explore the discipline's distant and recent past in order to rethink its missions and methods today.

Group Psychotherapy and Recovery From Addiction: Carrying the Message by Jeffrey D. Roth, M.D. '78 (Haworth Press) This book examines recovery, demonstrating the elements of the group process, including free association, resistance, transference and boundary management, and lets readers compare and contrast participation in a psychotherapy group and in a Twelve Step group.

Experiences of Depression: Theoretical, Clinical, and Research Perspectives by Sidney J. Blatt, Ph.D., professor of psychiatry and psychology (APA Books) Using clinical examples and empirical investigations, Blatt demonstrates the value of considering the psychological dimensions of depression. He identifies two primary sources of depression: feelings of loneliness and abandonment and feelings of failure and worthlessness. Understanding these differences helps to elucidate the nature, etiology and treatment of the disorder.

Field Guide to Internal Medicine by David S. Smith, M.D., associate clinical professor of medicine, Lynn E. Sullivan, M.D. '96, assistant clinical professor of medicine, and Seonaid F. Hay, M.D., assistant professor of medicine (Lippincott Williams & Wilkins) This volume offers an overview of internal medicine, including discussions of pathophysiology, clinical presentation, diagnosis and management of medical emergencies and the most common diseases encountered among hospitalized patients.

The descriptions above are based on information from the publishers.

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

Library keeps a watchful eye on what works on the Web

In days of yore—before the year 2000, that is—libraries generally set up websites for their patrons “and assumed everyone could use them without a problem,” recalls Richard Zwies, M.L.I.S., Web services librarian at the Cushing/Whitney Medical Library.

Those days are over. A new research genre, based on usability studies, reflects libraries' growing interest in streamlining their websites. Usability studies test how easily users can navigate a site, whether their aim is to scan the contents of the latest issue of a journal, track down an article or find out if a book is on the shelf. If a study shows that users are confused, librarians can change labels or reconfigure links.

The new approach has caught on fast. When the Association of Research Libraries offered an interactive Web-based class on usability studies last fall, 72 of its 123 member libraries, including Yale, signed up for the 90-minute session.

“The virtual front door of the library is becoming more important than our actual, physical front door,” says Zwies. In the 2003-2004 academic year, researchers, physicians, students and other users knocked on that front door—the Cushing/Whitney home page—more than 4.4 million times. In comparison, people walked into the library 329,000 times that year. Zwies says people use the Web for research because it's accessible from almost anywhere, day and night.

Zwies just completed a small usability study of the medical library home page. He timed five volunteer testers as they tracked down several types of information. Zwies also counted the number of visitors to the “front door” for a week: users clicked on it 30,000 times. The most popular link? Webmail. Zwies actually finds that encouraging, as it suggests that many people at Yale set their browsers to the library home page. The second most popular link was to electronic journals.

The study showed that the site is generally easy to navigate, so Zwies plans only small changes. Even for this minor redesign, which eliminated redundant links, he sketched a new “wire frame,” Web parlance for the site's “bone structure.” He then passed that on to Web designer Patrick J. Lynch, director of the MedMedia Group at ITS-Med, saying, “... it's like a rough skeleton and Pat puts flesh on it.” (The home page already has some flesh on it, by the way: a woodcut of a cadaver, taken from the 16th-century anatomist Andreas Vesalius' *De Humani Corporis Fabrica*. Visit <http://info.med.yale.edu/library/>.)

Usability testing will be a perennial task, says Zwies. “As Web technologies arise that might be useful to our patrons' research, we will want to test them on human beings. We will be testing and tweaking, testing and tweaking.”

—Cathy Shufro



STANFORD UNIVERSITY

PAUL BERG**What role for the states in stem cell research?**

When scientists wanted to discuss the safety of recombinant DNA technologies in the mid-1970s, they convened the Asilomar Conference, where they agreed on guidelines that would minimize risk while allowing the research to blossom, said Stanford biochemist Paul Berg, PH.D. The first researcher to combine DNA from two different species, Berg shared the 1980 Nobel Prize in chemistry.

Berg doubts that a conference could resolve the current dispute about human embryonic stem cell research, because it centers not on science but on politics, ideology and moral beliefs. The Bush administration limits federal funding for research to a handful of embryonic stem cell lines, and Congress may even criminalize some therapeutic stem cell research. The pending legislation, said Berg in a September talk sponsored by the Bioethics and Public Policy Seminar Series, would deny 290 million American people access to potential therapies.

Berg supports efforts such as the recent ballot initiative approved by voters in November in California, which opened the way for state funding of stem cell research. "There is a role for the state to act for the welfare of its citizens," he said.

—C.S.

**MARIALE HARDIMAN****A molecular link between the brain and learning**

"When axons send signals that are received by dendrites, learning is taking place," said Mariale M. Hardiman, ED.D., the principal of a high-achieving public elementary/middle school in Baltimore and a speaker at a symposium in October celebrating the 35th anniversary of the Yale Child Study Center's Comer School Development Program (See "Leaving No Child Behind," p. 24).

"We know that [making a] connection is important," Hardiman said, citing the way a teacher and student may connect in the classroom. "What is fascinating is that it is happening on a molecular level."

Hardiman has developed a "brain-targeted teaching" model that applies neuroscience to teaching. Teaching, she said, is most effective when it builds on what students know and prods them to learn more as they embark on a task.

Unfortunately, said Hardiman, the No Child Left Behind Act favors higher test scores over activities that require higher-order thinking. "What I see across the country is that education is moving back to a time when teaching was primarily test- and textbook-driven. While this traditional style of teaching has a place in our educational system, brain research seems to support more active, experiential teaching and learning," she said.

—John Curtis

**ROBERT BALLARD****Using revolutionary technology to find "a rusty old ship"**

After he discovered the wreck of Titanic in 1985, Robert D. Ballard, PH.D., heard from his mother. "That's all they're going to remember you for," she said, "having found a rusty old ship."

Since then Ballard, founder and president of the Institute for Exploration at Mystic Aquarium, where he works with Dean Emeritus Gerard N. Burrow, M.D. '58, HS '66, has gone on to find PT 109 and Roman trading ships, among others. But his real accomplishment in finding the Titanic was the validation of a new approach to exploring the 72 percent of the Earth under the sea. Frustrated by the limitations of sending people underwater, he developed a telepresence—remotely operated vehicles with sophisticated digital cameras. "It had all the characteristics of my submarine, except me," he said in October during the Wayne O. Southwick Lecture for the Department of Orthopaedics and Rehabilitation. "The first application of this new exploratory technology was the discovery of the Titanic."

When he saw the high degree of preservation on the ship—including a chandelier still hanging in the ballroom—he came to another realization. "It hadn't dawned on me that the sea was a museum," he said.

—J.C.



JOHN CURTIS (3)

RACHEL COHEN**A moral argument for fighting diseases of the poor**

Rachel M. Cohen called for a new approach to drug research and development based on need, not profit, in a September talk sponsored by the Justice and the Allocation of Health Care working group of the Yale Interdisciplinary Bioethics Project.

"We have made a societal choice that drug development should be confined to the private sector and that medicines are a commodity like any other that should be developed in order to maximize profit," said Cohen, U.S. director of the Doctors Without Borders/Médecins Sans Frontières Campaign for Access to Essential Medicines. As a result, most new drugs benefit inhabitants of the world's richest nations and little is invested in drugs for diseases of the developing world, such as tuberculosis and malaria.

"Well, we're sick of it," she said, calling for a global framework that would define a health agenda, commit wealthy nations to contribute to health care internationally and strengthen international mechanisms for exchanging research results. "Our patients are dying, and we need to change the rules. We need a needs-driven global approach to thinking about how to finance research and development, with a general acknowledgement that research is failing poor people."

—J.C.

THIS PAGE Societal notions of what constitutes a healthy body weight and pleasing form have varied greatly over the centuries, and it is only in eras of nutritional abundance that anxieties about the effects of too much food have figured prominently in the public psyche. Scarcity was the overriding concern of millions of Americans who struggled to find enough to eat during the Great Depression, such as these New Yorkers waiting for bread.

From scarcity to plenty since Colonial days

A Yale medical historian studies how famine and feast influence our bodies and how we view them.

FARM SECURITY ADMINISTRATION / LIBRARY OF CONGRESS

By Cathy Shufro

Living as we do in the “low-carb nation”—where, despite the gospel according to Atkins, obesity rates are escalating—it’s easy to forget that as recently as the 1930s many Americans worried about eating too little, not too much.

Yale medical historian Susan E. Lederer, PH.D., sees the end of World War II as a turning point. Until then, scarcity dominated people’s anxieties. Now, we worry about the effects of abundance on our bodies. Given her scholarly perspective, you’d think Lederer might have anticipated that even her daughter might be affected by “an ideal [of thinness] that virtually no one can achieve.” But when five-year-old Emma declined to sample a

Flintstones vitamin after seeing a picture of a chubby baby Pebbles (“It’s going to make me fat.”), Lederer recalls, “I was really kind of stunned.”

That incident, in part, inspired the associate professor of the history of medicine to offer a course at Yale College called “Fat and Thin: A History of American Bodies.” Lederer expected 50 to 75 students, and she ended up with 358. She had to expand her team of teaching fellows from two to nine.

The course, offered last spring, surveyed the evolution since Colonial times of notions of nutrition, food choices and ideal body weight, and how both scarcity and plenty can mark the body. The story began with scarcity. Although Native Americans had

developed strategies to avoid famine, by following food or by storing it, European newcomers arrived unprepared. In a 1607 diary entry, Jamestown settler Master George Percy describes his group’s reprieve from hunger: “It pleased God, after a while, to send those people which were our mortall enemies to releev us with victuals, as Bread, Corne, Fish and Flesh in great plentie. ... Otherwise we had all perished.” During the winter of 1609-1610, 80 percent of the Jamestown settlers did perish, of starvation and sickness.

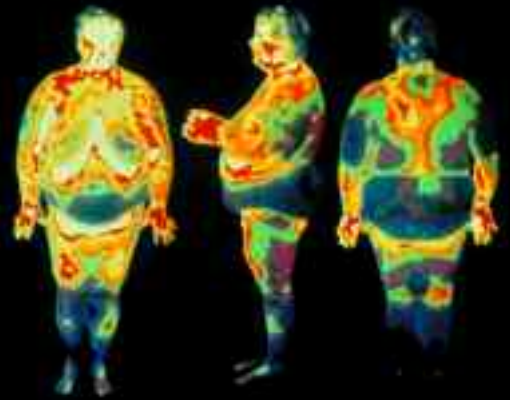
Three centuries later, Lederer’s students learned, scarcity still marked the bodies of Americans. In the South, prisoners and orphans suffered from

BELOW The subjects of Flemish painter Peter Paul Rubens' canvases were amply endowed with body fat—a sign of beauty, good health and prosperity—as seen in this version of *The Judgment of Paris*, circa 1635-1638. In the New World, where famine struck the Jamestown settlement three decades earlier, colonists would have been grateful to emulate them.



ERICH LESSING / ART RESOURCE, NY

RIGHT AND BELOW RIGHT In the 1940s, promoting proper nutrition was the aim of this poster produced by the Works Projects Administration. By the end of the 20th century, Americans had become obsessed with thinness—and fatter than ever—as they looked to medicine, fad diets and technology to solve the problem. Here, three thermograms of an obese woman show the distribution of both heat and body fat.



TOP WPA POSTER COLLECTION / LIBRARY OF CONGRESS
ABOVE RAY CLARK AND MERVYN GOFF / PHOTO RESEARCHERS

“the four D’s” of pellagra—dermatitis, diarrhea, dementia and death. U.S. Public Health Service physician Joseph Goldberger, M.D., set out to prove that pellagra resulted from their cornmeal-based diet. In his 1915 Rankin prison farm experiment, he induced pellagra in convicts in return for clemency. (Except for one protest, the only objection to this experiment came from those who were upset that convicts in prison for serious crimes were released in return for their participation.) Even then, he failed to convince detractors that the disease was caused by a diet deficient in niacin, not by microbes.

The contemporary obesity epidemic derives in part from the plethora of manufactured snacks, says Lederer. In

the 1920s, she notes, ready-made snacks were few: popcorn, Graham crackers, biscuits, penny candy. “Now we have more food choices than anyone else on the planet, and we’re so conflicted over them,” she says. When researchers asked people what they associate with a slice of double-chocolate cake, French respondents said “Celebration.” Americans said “Guilt.”

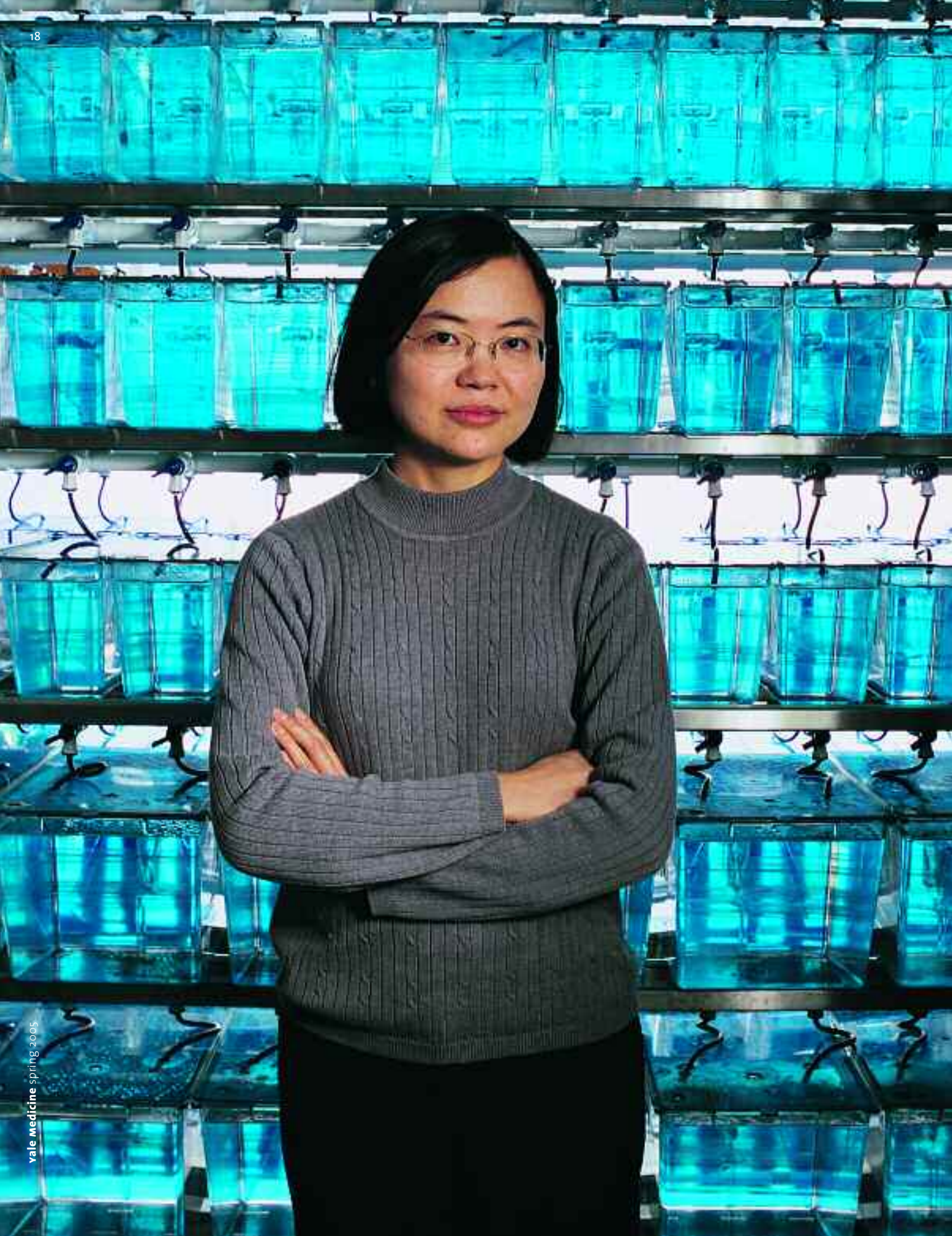
A study of 2,600 elementary school children in New York City, reported by the city’s health department in 2004, found that 40 percent were overweight, and one in four was obese. Hispanic children were most likely to be overweight and Asian students were least likely.

Among Yale students, Lederer says, “There’s a lot of interest in bodies,” espe-

cially among athletes. Twenty-five women from the Yale track team enrolled in the course, along with football player Nate Lawrie, a senior who was drafted by the Tampa Bay Buccaneers last spring. The caption next to Lawrie’s photo on the team’s website reads: “TE Nate Lawrie has the frame to add weight without sacrificing speed.”

For historical perspective on obesity, Lederer uses a cartoon from *The New Yorker*. Two witches watch as a plump boy and girl walk by the witches’ candy-festooned gingerbread cottage. One witch asks the other: “Remember when we used to have to fatten the kids up first?”

Cathy Shufro is a contributing editor of *Yale Medicine*.



Lessons from the depths

By Jennifer Kaylin

Photographs by Frank Poole

Accounts of death row inmates released from prison based on DNA evidence have become as routine as news stories about celebrity births, betrothals and breakups. On television, the popularity of shows such as *CSI*, *Crossing Jordan* and *Cold Case Files* attests to the public's familiarity with this field of research.

In 1983 Kary B. Mullis, PH.D., who 10 years later was a co-winner of a Nobel Prize in chemistry for his discovery, enabled this revolutionary application of genetic science with a method called polymerase chain reaction (PCR), which allows scientists to analyze DNA samples by generating copies of a genetic fragment. But the process, which relies on the enzyme polymerase, was as time-consuming as it was groundbreaking. DNA strands had to be unwound and separated through a three-step process involving about 40 heating and cooling cycles. It wasn't until scientists figured out how to streamline the technique, through a method called rapid automated PCR, that it became the medical and forensic bonanza

Scientists are increasingly turning to aquatic organisms as they seek clues to human physiology and disease. Zebrafish, coral and sea hares are becoming model organisms on a par with *Drosophila*, mice and yeast.

it is today. What made the breakthrough possible was the identification of a bacterium, *Thermus aquaticus*, which thrives in hot springs. Its polymerase can survive temperatures that fluctuate between 72 and 90 degrees Celsius.

This is just one example of how scientists have expanded research capabilities by shifting their gaze from earth to water.

The guinea pig was once synonymous with biological research. Rats and mice are still ubiquitous in research labs, but researchers are increasingly pulling up anchor to find aquatic animal models that might offer better solutions to specific research questions. At Yale several scientists are embracing their potential, using aquatic specimens to study everything from liver and kidney diseases to neurophysiology and the effects of toxic substances on living organisms.

James L. Boyer, M.D., HS '67, FW '69, director of Yale's Liver Center, has spent the last 33 summers conducting research at the Mount Desert Island Biological Laboratory in Salsbury Cove, Maine. Recently Boyer has been studying

Zhaoxia Sun, who studies the genetic causes of polycystic kidney disease, keeps thousands of zebrafish in her laboratory in the School of Medicine. Also known by the Latin name *Brachydanio rerio*, zebrafish have emerged in recent years as a model organism for basic research relevant to human disease.

the skate liver to see how it sheds itself of toxic substances. He initially used the livers of dogfish sharks, but found the skate liver easier to handle and more mammalian in size and shape.

Boyer, who is the director of the Comparative Toxicogenomics Database at the Mount Desert Island facility, says scientists long believed that if you wanted to learn about human biology, you had to study other mammals. Now researchers are finding that studying less-similar creatures can also be illuminating. “By comparing our genes with the genes of lower vertebrates we can often get a better estimate of what the most important parts of our genes are, because the differences are greater than when we compare our genes with genes of a mouse or other mammal, which are very similar if not nearly identical,” he says.

According to Boyer, the most famous example of an aquatic specimen shedding light on human physiology is the squid axon, which is so large that when scientists probe it with electrodes they can easily see how nerves conduct signals. Another is the sea slug. With its large cells, it has helped scientists understand signaling pathways in nerve tissues.

At the Mount Desert Island lab, scientists have spent years studying the rectal gland of the dogfish shark. This gland has one job only—to pump salt. Their research has provided insights into such diseases as cystic fibrosis, which stems from a salt imbalance caused by the body’s inability to regulate chloride transport. “There are many examples of this type of story,” Boyer says, “but it’s not yet appreciated how useful these species can be.” Aquatic animal research has lagged, he says, partly because the study of marine specimens requires travel to remote locations as well as special facilities and equipment.

The search for clues to human physiology in the sea dates to the early 20th century, when scientists, inspired by Darwin, founded marine biology labs, including the Mount Desert Island facility and the Woods Hole Oceanographic Institution in Massachusetts, along the East Coast. But, according to Boyer, it wasn’t until the genetic revolution—the cloning and sequencing of genes—that the use of marine specimens for research really gained currency.

“Through comparisons of genes from lower organisms with human genes, we demonstrated that our genetic material was more similar to these lower vertebrates than we thought,” Boyer says. The gene that codes for the bile salt export pump in the skate liver, for example, is

70 percent identical at the amino acid level to the human gene. “We find that all of the human mutations occur in the same regions that are identical between skate and man,” Boyer says. “Thus, we are beginning to learn that the 30 percent of our bile salt export gene that is different from the skate is not very important from a functional point of view.”

Scientists now have a pretty good library of mammalian cell lines, but according to Boyer, similar models need to be developed in aquatic animals. That is a priority for researchers at the Mount Desert Island lab, who have a grant from the National Institute of Environmental Health Sciences to create the Comparative Toxicogenomics Database.

A new model from India

The current poster fish for aquatic animal research is the zebrafish, a small freshwater fish originally found in slow streams and rice paddies in the Ganges River in India. In the early 1970s, George Streisinger, PH.D., at the University of Oregon, determined that zebrafish were an invaluable model for studying vertebrate development and genetics. Since then, their embryos have been used worldwide to study how all vertebrates, including humans, develop.

What makes the zebrafish ideal is their eggs—they are transparent and they develop outside the mother’s body. And while a mouse takes 21 days to develop, zebrafish grow from a single cell into a tiny fish within 24 hours. Scientists can watch under the microscope as the zebrafish cells divide and form different parts of the infant fish’s body. Scientists can easily move or destroy a cell to see what happens. And zebrafish, like humans, have a backbone, making them more similar to humans than commonly studied invertebrates such as *Drosophila* and *C. elegans*.

Zebrafish are also easy and relatively inexpensive to maintain, manipulate and monitor in the lab. This makes large-scale studies far more feasible and affordable. They thrive in many environments, can be kept together in large numbers, are easy to breed and require less stringent research protocols than mammals. In fact, the zebrafish has become so popular in recent years that it has its own magazine, *Zebrafish*, and, like all celebrities, its own website, www.zfin.org.

Zhaoxia Sun, PH.D. ’98, established the first zebrafish facility at the School of Medicine in 2003 in a former auto-clave dishwashing room down the hall from her lab. It now

resembles an aquarium, with shelf upon shelf of shoebox-sized tanks, each swarming with tiny striped fish. Sun, an assistant professor of genetics, returned to New Haven in 2003 from a postdoctoral fellowship at the Massachusetts Institute of Technology, where she used zebrafish to explore the genetic causes of polycystic kidney disease.

“Zebrafish provide so many unique features,” Sun says. “So many things not previously possible are now possible.” In collaboration with researchers at MIT, she performed a large-scale zebrafish screen and identified 12 genes that, when defective, can cause polycystic kidney disease. “It would have taken a lot longer without the zebrafish,” Sun says.

Her zebrafish studies are starting to attract the attention of other Yale researchers, and she has received inquiries from faculty in nephrology, physiology, genetics and cardiol-

For the past 33 years James Boyer, below left, has spent his summers on Maine’s Mount Desert Island, where he has used dogfish sharks and other fish to explore human physiology. Boyer, who directs the Liver Center at Yale, is studying the liver of the skate to see how it rids itself of toxic substances.

Leonard Kaczmarek has long used marine organisms for his research into nerve cell function. One of his favorites is the sea hare, which has nerve cells large enough to be seen with the naked eye.



ogy about possible collaborations. She welcomes these opportunities. “I think zebrafish will be helpful in bridging different fields,” she says. “It’s still a young field, but it’s a field with huge potential.”

Across campus, Scott A. Holley, PH.D., assistant professor of molecular, cellular and developmental biology, is the only other Yale scientist working exclusively with zebrafish. Holley, who studies early vertebrate development and genes related to skeletal defects, meets regularly with Sun, and the two plan to teach a course together. “The field is in a rapid growth phase,” says Holley, noting that at his first zebrafish conference in 1997 about 120 scientists attended. At a meeting in 2004, attendance topped 1,000.

A tool from the coral reefs

Vincent A. Pieribone, PH.D., associate professor of cellular and molecular physiology and neurobiology, credits the green fluorescent protein (GFP) found in *Aequorea victoria* jellyfish with revolutionizing his studies of how the human brain works. He wanted to see how collections of nerve cells fire, but the density of cells in the mammalian brain and the speed at which they fire make it next to impossible, and recording one cell at a time “was like listening to an individual phone line in New York City and trying to

FROM LEFT Fluorescent proteins in corals such as *Lobophyllia hawaii* respond to a blue excitation light. Like *Lobophyllia*, the *Acropora tenuis* coral also has both green and red fluorescent proteins that respond to

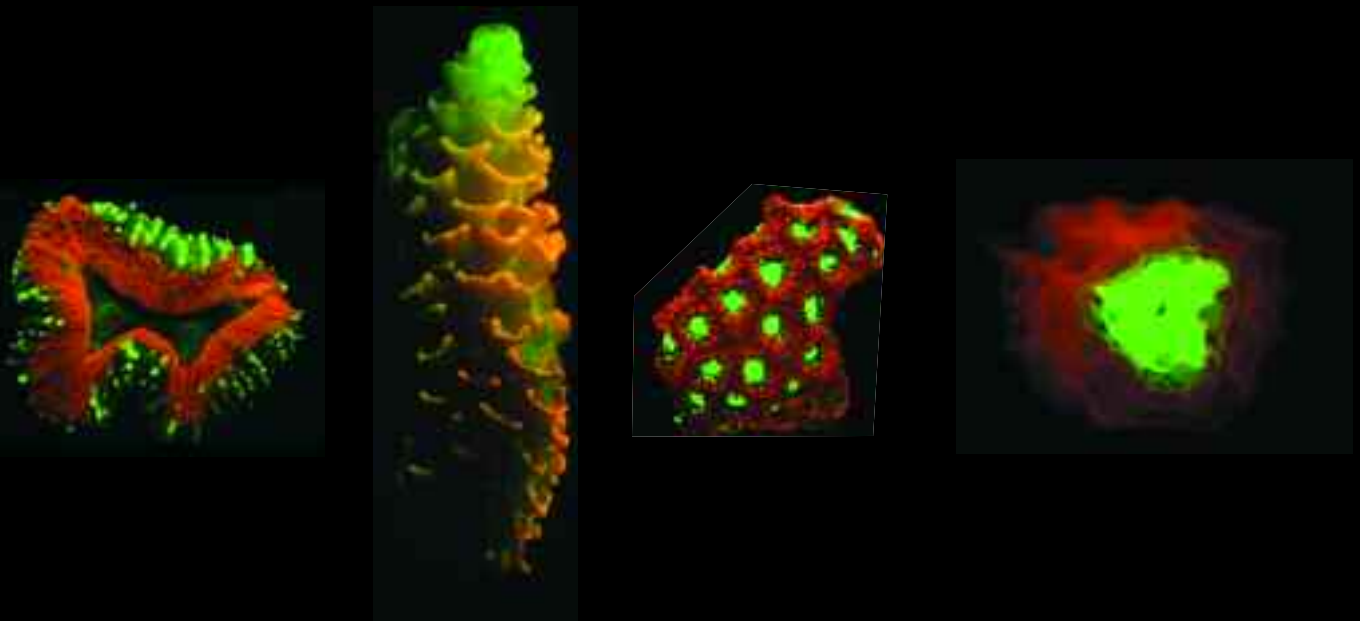
blue light. Blue light brings out the fluorescence in this high-power image of a polyp from a species of *Goniastrea* coral. The same coral seen at low power.

figure out from that how the city functions,” he says. Plus there was the challenge of recording what was happening without resorting to invasive, damaging procedures.

Enter GFP. “You can put it into any cell in any animal and the cell will fluoresce green and be identifiable,” Pieribone says. “It’s been hugely important to scientific study.” GFP has been used to track cells in a wide range of animals and has enabled scientists to watch cells develop in real time without having to kill the specimen. Kaeda-type GFPs have taken the promise of this research tool one step further, because they work as “reporters.” “They don’t just tag cells,” Pieribone says. “They can be made to change color (from green to red), allowing scientists to monitor the movement and synthesis of the protein.” Pieribone’s laboratory is focused on fusing GFPs to other proteins that cause the fluorescence emission of GFP to be altered by a cellular process. “This tells us what’s going on—is the calcium going up, for instance—when the cells do what they do.”

The success of GFP from jellyfish prompted scientists to return to the sea in search of proteins in other colors. In June 2001, on Lizard Island, part of the Great Barrier Reef in Australia, Pieribone and his colleagues identified two corals (*Lobophyllia hemprichii* and *Flavites* spp.) that produce fluorescent proteins. One glows red; the other switches

VINCENT PIERIBONE



from green to red when exposed to UV light.

“A lot of biological specimens have backgrounds that fluoresce a kind of greenish glow,” Pieribone says, “so with these new fluorescent proteins, things stand out better. They’re a lot easier to see.”

In all, he has identified about 40 species of fluorescent coral. The two GFPs Pieribone and his colleagues cloned are not currently in use, but others like it are. Besides corals and jellyfish, scientists have also cloned GFP-like sequences from anemones, sea pansies, sea pens and copapods, bringing the total number to around 70.

Along with new fluorescent proteins, Pieribone also found that coral reefs the world over are dying, which he says would be a huge loss for science, to say nothing of the ecological ramifications. “When we lose these reefs, we’ve lost an amazing library of genes,” Pieribone says. To save what he and other scientists consider a vital resource, Pieribone is trying to apply biomedical technology to understand how global warming is killing the corals. While this is a diversion from his work as a neurophysiologist, he says there’s an important connection. “Nature makes mutations that can be cloned and studied for utility in the laboratory,” he says. “If we kill the animals, we lose that ancient library and we don’t have millions of years to wait around for another to be formed.”

Pieribone’s work with aquatic specimens prompted him in September 2003 to found Marinus Pharmaceuticals, based in Branford, Conn., which has seven employees. The company seeks to use information gathered through marine research to create drugs to treat epilepsy, depression, schizophrenia and heart disease. “The environment in the ocean is harsh. Organisms that have adapted to survive there are very tough,” he says. “They have a lot to teach us about survival strategies.”

Sea hares and nerves of steel

As a researcher who studies nerve cell function, Leonard K. Kaczmarek, PH.D., professor of pharmacology and cellular and molecular physiology, is particularly fond of the squid and the sea hare. Their main appeal is their large cells. Some of the sea hare’s nerve cells, for example, can be seen with the naked eye. “They’re also color-coded, from white to bright orange,” Kaczmarek says, “so you can give each one a name and number. It’s very easy to figure out how nerves control behaviors.” Sea hares are also desirable research specimens because their cells are so hardy. “The human brain, if deprived

of oxygen, dies in a few minutes,” Kaczmarek says. “Sea hare nerve cells have been known to live up to a week.” Using this species, Kaczmarek is studying bag cell neurons, which serve as a master switch for the control of reproductive behaviors.

Despite the differences between humans and marine organisms, the way nerve cells respond to the outside world and generate electrical activity that controls behavior is highly conserved across evolution. For example, many ion channels—the proteins that control the electrical behavior of neurons—are almost identical in molluscs and humans.

The main attraction of the squid, Kaczmarek says, is that its synapses are so large they can be seen without a microscope. Many human synapses are round and measure 1 to 2 microns in diameter. The squid giant synapse is 300 microns wide and as long as a millimeter. “It makes it very easy to study how one neuron can stimulate another neuron. It also allows us to investigate ion channels in different parts of the synapse in ways that are simply not possible with mammalian cells.”

Although he uses rats and mice for most of his research, Kaczmarek sees himself continuing to study sea animals for the foreseeable future. “So many breakthroughs happen with simple model systems,” he says. “Besides, it’s very nice to have both perspectives.”

Like Boyer and Pieribone, Kaczmarek worries that funding, fashion or affronts to the environment could threaten marine animal research. This, he says, would be a shame. Noting that research based on squid led to Nobel prizes in 1963 and 1970, he says, “Just look at the history. It’s very obvious that looking at really simple systems gives insights into understanding more complicated systems.” **YM**

Jennifer Kaylin is a writer in New Haven.

Frank Poole is a photographer in New Haven.

Leaving no child behind

In a memoir of his formative years, child psychiatrist James Comer describes what he learned from his family and neighbors—and how he sought to make those values the linchpin of an educational philosophy.

In 1968 a newly minted psychiatrist at the Child Study Center began working on a plan to help two underachieving elementary schools in New Haven. Behind this effort was his belief that, regardless of race, geography or background, all children can learn at high levels. Now known as the School Development Program, referred to more familiarly as “the Comer process” or “the Comer model,” the young doctor’s vision is in practice in more than 600 schools in 20 states. The Comer model celebrated its 35th anniversary in October with a symposium that explored brain research and its implications for child development, education and teacher preparation. At the program’s 30th anniversary in 1999, First Lady Hillary Rodham Clinton, who interned at the Child Study Center while a law student at Yale, was the keynote speaker.

The program’s namesake, James P. Comer, M.D., HS ’66, M.P.H., the Maurice Falk Professor of Child Psychiatry in the Child Study

Center, applied the lessons he learned as a child growing up in a nurturing environment of family, church and neighborhood. His program takes into account the developmental needs of children, as well as their social environment. At its heart is a strengthening of the bonds among families, schools and neighborhoods—relationships that were crucial to Comer during his youth in industrial northern Indiana. No school stands alone, Comer believes, and in order to succeed, each school needs to work with other community institutions.

In his book *Leave No Child Behind: Preparing Today’s Youth for Tomorrow’s World*, published last summer, Comer tells the story of his program, how it started, how it nearly failed and how, ultimately, it succeeded. In this excerpt, Comer describes the values he and his siblings learned from his church, his neighbors and, most of all, his parents.

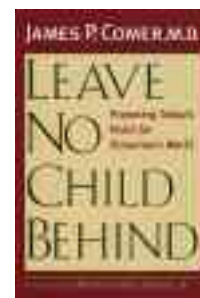
I went off to kindergarten with three black friends who were as bright as anybody in my family and anyone in our school. They went on a downhill course in school and in life despite the fact that our parents had the same level of education and similar jobs and we were in the same good school. My siblings and I went on to earn a collective total of 13 university degrees. Eventually I realized that the only difference between my siblings and me and our three friends was the quality of the child-rearing and developmental experience that we received at home and in our primary social network of friends, kin and organizations in which our family felt a sense of belonging—namely, our church.

My siblings and I were born into a family in which we were very much wanted and valued, and our parents were skillful child-rearers. This was the case despite my mother’s



LEFT At the Columbus School in New Haven's Fair Haven neighborhood, James Comer visits a classroom where teachers, teachers' aides and parents employ an approach to reading that is part of his School Development Program.

BELOW In a family photo taken at his childhood home in Indiana, Comer poses with his parents and siblings.



own difficult upbringing and the limited school time of both. My mother was born into extreme poverty in rural Mississippi. She was the third of five children, and her father had two children from a previous marriage. Her father was a good man who loved and provided for his family. But when she was 6 years of age, in 1910, he was killed by lightning. Because the children were too small to help with the work, a cruel stepfather came into their lives. There were two more children from this marriage, nine in all. They moved from place to place, living in one shack after another; and he unexpectedly abandoned the family from time to time. Also, he was abusive in many ways and would not let the children go to school.

When my mother, Maggie, was 8 years of age, it occurred to her that the way to a better life was through edu-

cation. When she was 16, she ran away to a sister in East Chicago, Ind., with the hope of going to school. But her sister could see no benefit in a "colored girl getting an education" and was not supportive. After several months, she had to drop out of school. She began to do domestic work. When she left school she declared, "If I ever have children, I'm going to make certain that every one of them gets a good education!" Then she set out to very carefully find a like-minded husband.

He was 12 years older. They met in Sunday school—my father as teacher, my mother as student. He had been married once before and had a child, a reason for great caution given my mother's childhood experience. She only agreed to go out with him after his ex-mother-in-law wrote a letter of support. They were married two years later.



TOP Both his mother, Maggie, and father, Hugh, came from poor families in the South, and both believed that education was the key to a better life.

ABOVE Comer, second from right, with his sister and brothers, also dressed as soldiers.

My father, Hugh, was from rural Alabama, the son of a minister. He had about a sixth-grade rural Alabama education. His family was poor but well-functioning and in the process of buying their farm from the former slave master's heirs. To save the farm after boll weevils destroyed the crop in 1918, he left Alabama and worked in the steel mills in East Chicago. He, too, felt that the only way to a better life was through education.

They set out to have a family and to provide us with what they had not been able to acquire for themselves. But they were not in a hurry. It was 12 years before I was born. During that time my parents reared my older sister, Louise, my father's daughter. They were enmeshed in a church-based culture and community. And my mother continued to do domestic work for some of the most successful families in town. My father worked as a steel mill laborer, and they built their home with their own hands. Then we came, four of us—I was the oldest of three boys and a girl—almost one year apart over a five-year period.

A rich culture

As I describe our childhood, keep in mind the fertile ground in which we sank our roots—an emotionally rich church culture, exposure to and participation in the mainstream culture, parental ambition and a belief in the American dream of better opportunity for all, and just enough income to keep hope alive. And our parents had an understanding that children had to be prepared for a better future, and they delighted in doing so. As a result we received a great deal of *nurturance* from the very beginning.

In the summer, after work or on weekends, my mother and father would take us to Lake Front Park, where they would play with us, or sit and talk while we played. I still remember sitting on the front porch eating popcorn and drinking malted milks on warm summer evenings. Also, we were served ice-pops from the freezer. All of the snacks were homemade because it was less expensive, more fun and more personal.

Every Sunday evening my mother would read us the "Sunday funnies." Two of us would sit on her lap and two down in front. We would squeeze in as close to her as we could get. Each of us had a favorite column that we would ask her to read again until she had read the paper two or three times.

The funnies were not great literature, and my mother read at a second-grade level or less. But that was not important. The nurturance, emotional warmth and closeness that we received provided us with the beginnings of a powerful sense of belonging and security; again, the most important of human needs. And in the process, reading was given a powerful, positive emotional charge.

A reasonable sense of security and belonging fosters confidence and prepares children to take on the challenges of their environment and, with help and approval, gain competencies that enable them to successfully manage the chal-

lenges of their world. As they succeed they begin to feel, “I am somebody of worth, value and competence. I am. I can. I will.” These conditions, combined with the need for self-expression, are the foundation of motivation. Caretaker guidance helps make the process constructive.

A philosophical father and a pragmatic mother

We received the guidance, skills and values needed for appropriate social functioning and self-expression through many casual interactions, interactions that reflected our parents’ attitudes, beliefs and ways of approaching life. From my more philosophical father we often heard:

“If you can’t be the best, be among the best”—be competitive, excellent.

“Nothing beats a failure but a try”—initiative, effort, chance taking.

“A man’s word is his bond”—be responsible, show trustworthy behavior.

“The measure of a man is the way he treats his fellow man”—respectful relationships.

“Never let your race stop you from doing anything you want to do”—and much more.

And from my pragmatic mother:

“Be reasonable.”

“A procrastinator’s work is never done.”

“Never mind the teacher, you get it upstairs. They can’t take that away from you.”

“If you are on time, you are five minutes late.”

“Recognize trouble, and stay away from it.”

One of the places such mental and moral morsels were frequently served was at the dinner table. But dinner time was more than messages. We ate at the same time every evening—regularity. We were expected to talk about the things that went on during the day that might be of interest to everyone—reflection and reporting. Through subtle clues, sometimes insistent suggestions, we were asked not to talk too long, to give others a chance to speak, to listen to what they had to say—skills of conversation. Spontaneous discussions were encouraged, even strong emotions, but we were expected to keep emotions under reasonable control—free expression within limits and with self-control. Teasing was fine and fun, but you could not hurt anybody’s feelings too much—a family value. Pretending you were hurt to get sympathy was frowned upon—no victims here.

My mother prepared everyone’s favorite dish from time to time—collard greens, cherry pie, German chocolate cake, hot rolls, cube steak. Each child received special recognition on the day his or her favorite food was prepared and on birthdays—you are special and we celebrate each other. Sharing, cooperating and enjoying the success of brothers and sisters were encouraged. These practices discouraged jealousy. The product of all of this was a family environment of warmth, trust and mutual respect and appreciation.

Our parents, and sometimes friends, took us to the museums in Chicago, the zoo, the circus, Marshall Field department store during the Christmas season, the Chicago Cubs park and on other trips. When President Franklin Delano Roosevelt’s caravan came through town, we were there. There was much discussion about what was going on during these “field trips.” And before all such occasions, my mother gave us social interaction “suggestions.” “Talk enough to be interesting, but don’t tell all of your business.” And wisdom to reflect on: “If you talk too much, people will find out how big a fool you are.”

Solving problems by listening and watching

I learned effective ways of solving problems by listening to and watching my parents. Once I listened to my mother talking on the telephone with my principal, Ms. McFeely. A bully had knocked my brother Norman down and sat on him.

Norman bit the bully, through his pants, on the butt. During the conversation my mother never raised her voice. Initially I could hear the sound of the principal’s voice, but she gradually quieted down. My mother’s responses went something like this: “No, I don’t approve of my children fighting.” (Pause while listening.)

“But you said that the boy was a bully, bigger, and that he started the fight.” (Listening.) “While I don’t expect them to fight, I do tell them that they are not to let anybody walk over them (or sit on them)! Fight back if necessary!” (Listening.)

“Now, if there’s a medical bill we will pay for it.” (Listening.)

“Thank you for calling, and please let me know whenever there’s a problem.”

When I was about 3 or 4 years of age, our family doctor was called to treat me. When he left I said, “I’m going to be a doctor when I get to be a big man!” My parents responded by buying me a doctor’s kit and playing doctor with me—reminding me that the candy pills were for the patient, not the doctor.

A neighbor asked, “Why are you encouraging him to be a doctor? We’re poor people. You know he will never be a doctor!” My mother told her that if she said that again she would have to leave. These neighbors were African-Americans. Their comments reflect the high level of group- and self-deprecation and the low level of aspiration and hope that existed, and still exists, among many.

Self-doubt-producing experiences were and are even more common outside the family network. In the middle of my fourth-grade year, a student transferred into our class. She told me that she knew my mother. The reason turned out to be that my mother had worked as a domestic for her mother years before. By age 10 or 11, social status is an identity issue. Although children don’t think “social status,” they make observations and ask questions that help them place themselves in the scheme of things—how they are valued, where they stand as reflected by their house, car, race, religion, occupation of

their parents, and so on. Their conclusions can influence their aspirations and effort. My mother noted that I was a little troubled by knowledge of that previous relationship. The knowledge was a threat to my quest for a sense of adequacy, belonging and security.

She stopped what she was doing, looked me in the eye and said, “Don’t let that bother you none. You’re just as clean as she is. You’re just as smart as she is. And you can do just as well in school.” She paused and with a no-nonsense facial expression said, “And you had better!” Fortified by the positive sanction of one of the two most powerful people in my young world, I did well.

All of these experiences helped me grow along all the developmental pathways. Growth in the social-interactive, psychological-emotional and ethical areas or pathways is particularly important in complex social systems, but these are all but ignored by educators and policymakers. The often subtle, challenging social situation can have huge negative consequences for any student, and for minority students in particular because they face them more often. Without good preparation, such environments can become hurtful and limiting. With adequate preparation, young people can turn the negative to positive support, or at least not be harmed.

A problem I encountered in the 11th grade comes to mind. Grades were given at the end of 10 weeks and a final grade at the end of 20. At the end of the first 10 weeks, I was one and two points, respectively, behind the two white students who received As in our language arts course. I was almost 30 points ahead of the next-closest student, but I received a B. After being told that a B was a good grade and other palliative things, my teacher eventually said kindly, “I just don’t think you’re capable of making an A.” That was the end of the discussion. I knew exactly what that meant. The grade she gave me was an expression of her racial stereotyping.

I did not raise my voice. I did not even tell my parents. I worked very hard that next semester and earned all As, and the top score in her class. But I did not take a chance. Her class was my first in the morning. I told her that I had forgotten my grade book. I collected all my grades, all As, and went back to her at the end of the day. She gave me an A without comment.

During my senior year, when I was no longer in her class, she asked my advice about how she might help an African-American student whom she was concerned about. He was very smart but not working up to his potential. Perhaps our discussion the year before, and the way the incident was managed, helped her confront her bias. Let me hasten to add that almost all of my white teachers were just. Some went out of their way to make certain that I was treated fairly. I did not have a black teacher until I went to medical school.

Learning values in church

Our family was enmeshed in a church culture that generated and reinforced the set of attitudes, values and behaviors we lived by. Our church culture was in sync with the mainstream culture—personal excellence, hard work, a delayed reward, good relationships. The church-based culture affirmed our value when society did not do so at the necessary level.

My experiences at home and in our primary social network prepared me for school. They enabled me to elicit a positive response from school people, to attach and bond with them and with the program of the school. Doing well academically and doing well socially were our prime family and social-network values. And being involved in sports, the arts and student government could be expected because our family supported participation in any activities that were believed to be educational. In fact, at one point, all four of us were student council representatives from our respective classes.

As a result of the care that had been given to nurturing us in our early years, before we started school, and our resultant ability to elicit positive responses, our family, school staff, classmates and community all supported our growth along all the developmental pathways. My three friends mentioned above were not so well-prepared for school, did not elicit positive responses and began a downward course almost from the beginning.

An incident many years later provided me with support for my notion that student-staff attachment and bonding are important. When my mother was a patient in the hospital in 1990, Ms. Walsh, my first-grade teacher, was then a spry 80-plus-year-old hospital volunteer. When she saw me, she threw her arms around my neck and said, “Oh, my little James!” (I was 55 years old at the time, but you are always 6 years old to your first-grade teacher.) She then stepped back, looked me over and said, “Oh, we just loved the Comer children. You were so bright, so eager to learn, got along so well with other children,” and on and on.

She was describing the outcome of dedicated, skilled child-rearing interactions; good development; and a genetically determined potential that was at least at or above the modest threshold level necessary for school and life success. It was “all of the above,” not intelligence alone, that made our academic success possible. Good development and a supportive family and church-based primary social network made it possible to manage the environment of the schools we attended and the world beyond. **YM**

In a reading classroom at the Columbus School students move from one station to another as they approach stories by analyzing plot,

studying vocabulary and predicting the outcome. Teachers, aides and parents work with the children in small groups.



TERRY DAGRADI (4)

What's in a name?

No Child Left Behind. Leave No Child Behind. Two slogans almost alike but for one word and the placement of the others. One is the creation of progressive child advocates and the other comes from a presidential campaign.

It is no accident that James P. Comer, M.D., HS '66, M.P.H., the Maurice Falk Professor of Child

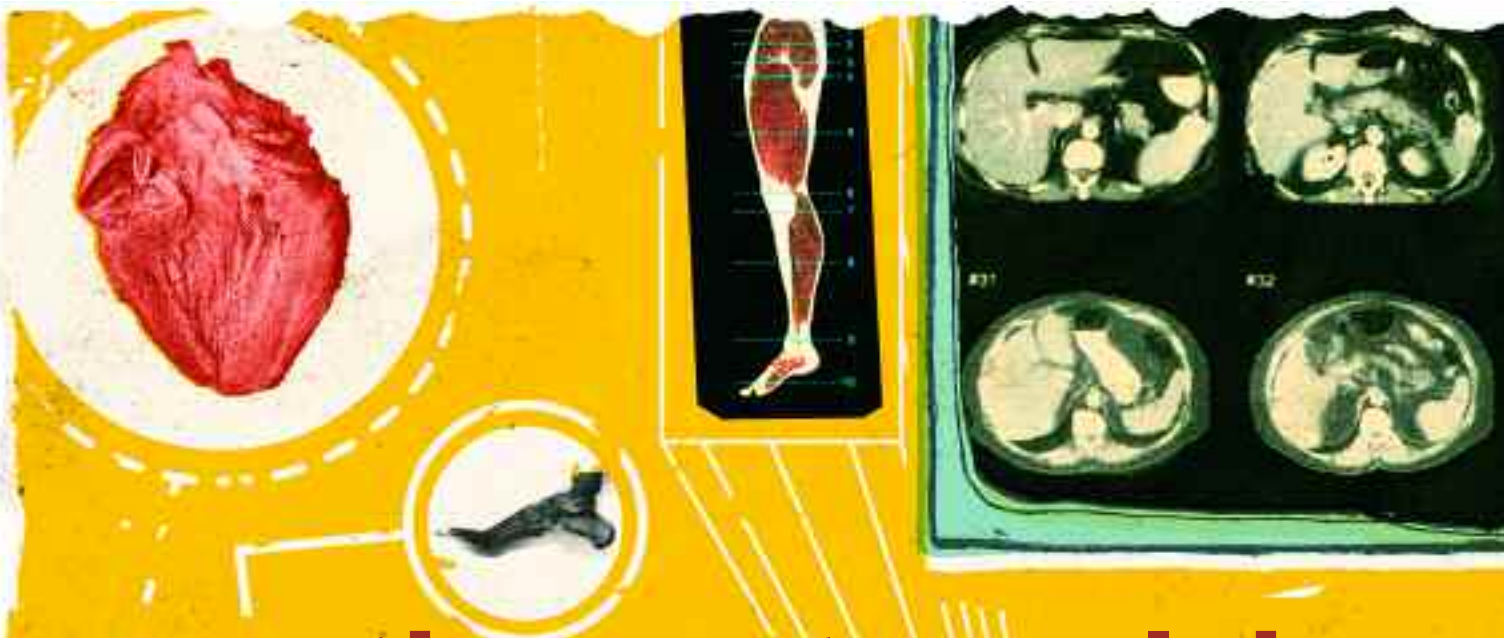
Psychiatry in the Child Study Center, chose *Leave No Child Behind* as the title of his latest book. It is the registered trademark of the Children's Defense Fund (CDF), which has worked since 1973 to ensure that children receive adequate education and health care.

During his 2000 campaign, President George W. Bush appropriated the slogan, much to the dismay of the CDF, which asked

Bush to "cease and desist" from using it. According to news accounts, the CDF even considered legal action to prevent those words from passing Bush's lips.

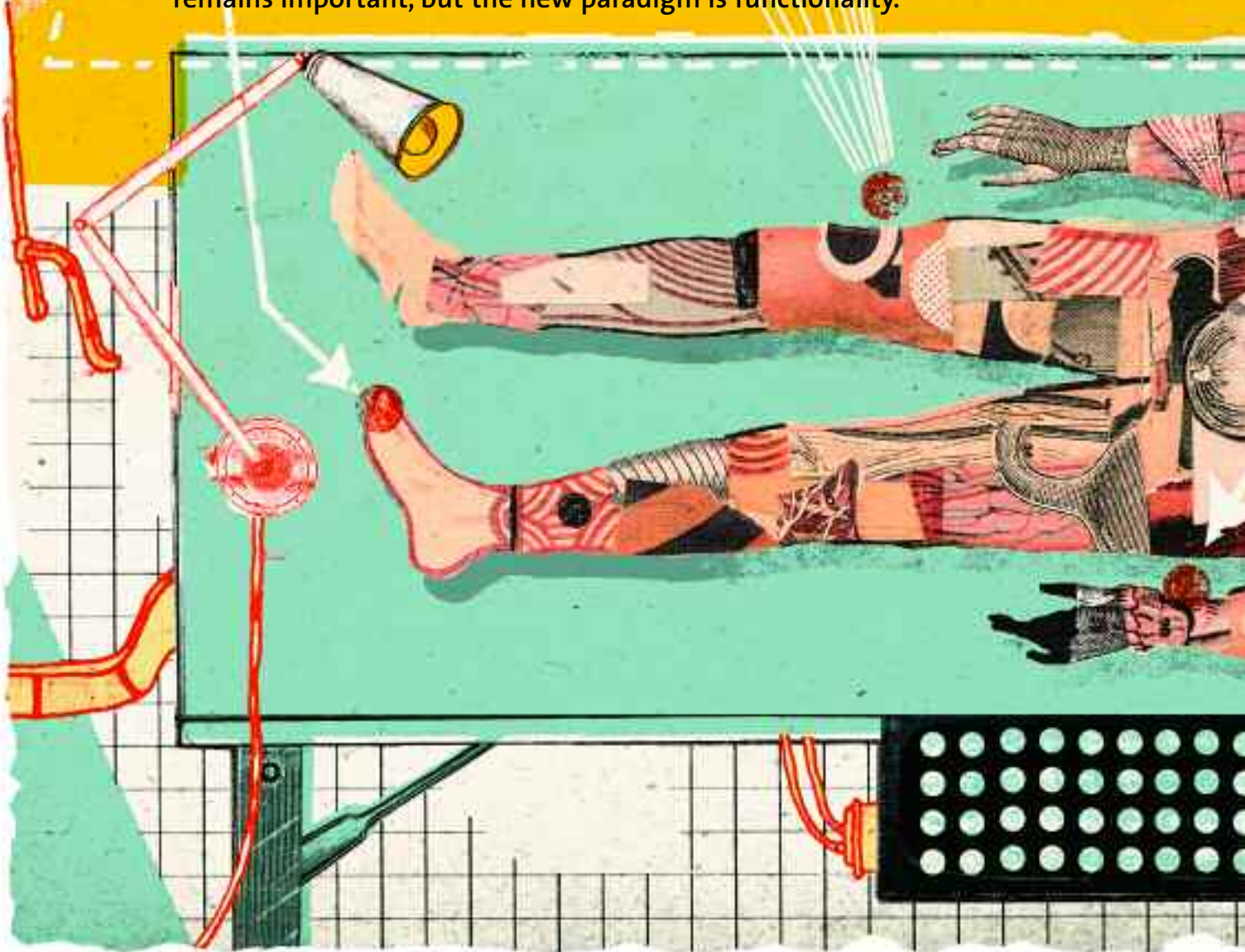
Comer's choice of *Leave No Child Behind* should not be seen as an endorsement of the act of Congress that carries a similar name. "The accountability piece of it is good," Comer said of the legislation, "but it goes about it in

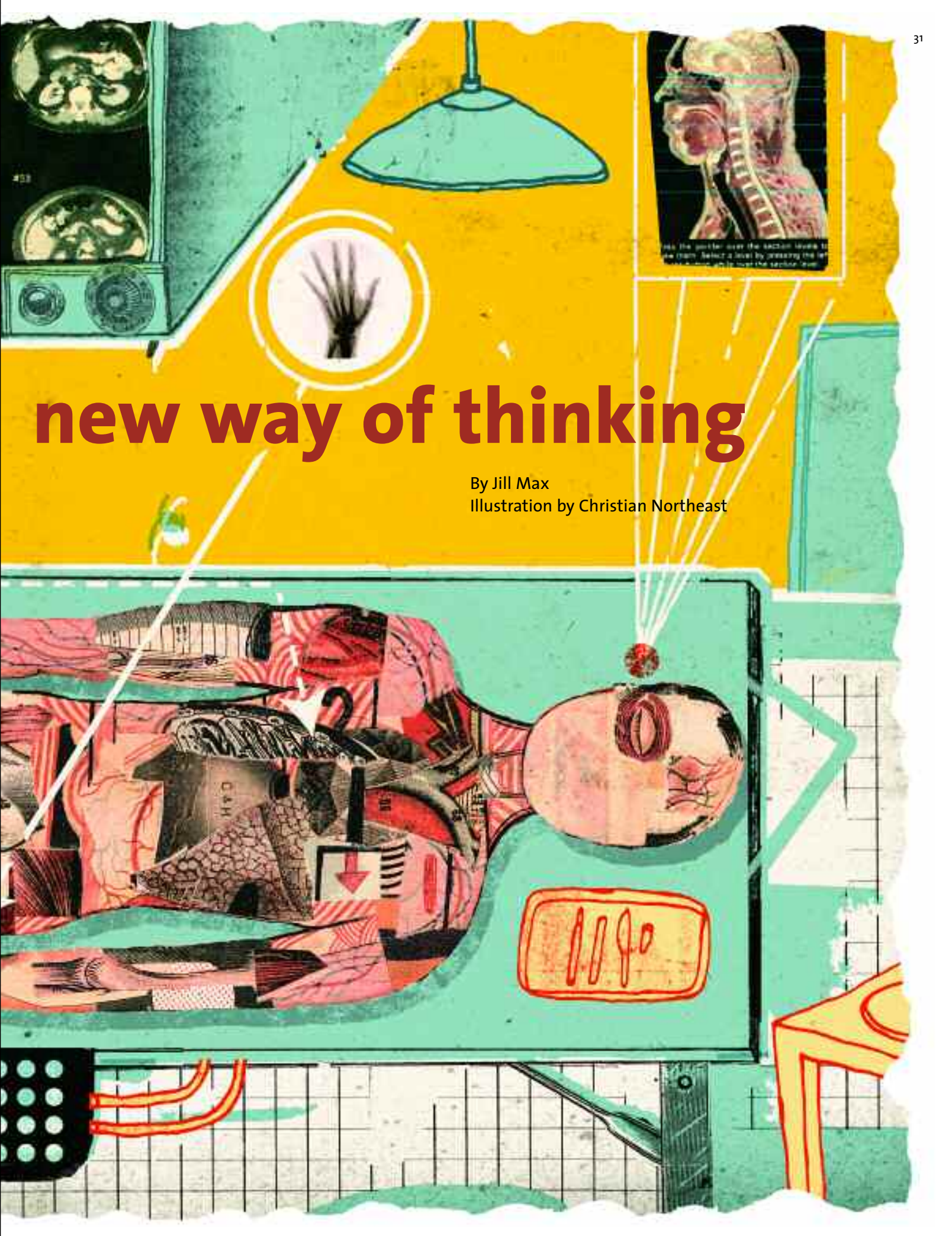
the wrong way, punishing rather than helping." The legislation, Comer believes, places enormous pressure on schools to "teach to the test" in order to meet accountability goals. Instead, Comer says, teachers should be encouraging students to learn along developmental pathways in a "friendly, warm, exciting environment."



In the anatomy lab, a

Scarce instructors, new tools and a boom in knowledge have led to an ongoing experiment in anatomy teaching. Structure remains important, but the new paradigm is functionality.





new way of thinking

By Jill Max
Illustration by Christian Northeast



Yale's fall semester has only been in session for about six weeks, but first-year medical student Jason Frangos is about to attempt surgery for a thoracic aortic aneurysm. He dons an apron and gloves, picks up a scalpel and prepares to make the first incision. "I'm afraid of

cutting something I don't want to cut," he says. It's a real concern, not because this is real surgery, but because it is an opportunity to learn: Frangos and his classmates are "operating" on cadavers for "Human Anatomy and Development," a course that is a rite of passage for medical students across the country. But while many of the basic elements of the course—preparation, dissection and lecture—have been in place for years, Yale's class of 2008 will learn anatomy in a way that is significantly different from that of past years.

The reasons for the shift are both practical and philosophical. Thanks to advances in medicine, students have more to learn in just about every field, and curricula are becoming more streamlined. While a classically taught anatomy course used to consist of upwards of 200 hours spread over two semesters, today's course is half that. At the same time, the pool of anatomy professors nationwide is dwindling, as young scientists turn to other disciplines in the life sciences where there are more abundant discoveries still to be made. According to a survey by the American Association of Anatomists (AAA), more than 80 percent of anatomy-related department chairs anticipate having "great" or "moderate" difficulty finding qualified faculty in the next few years. In response, medical schools have recruited professors from other departments, as well as physicians in the community. And a new concept has emerged to play an increasingly pivotal role in medical education at Yale—functionality. "The notion of a functional approach is a philosophy we've developed for dealing with the staggering amounts of information students have to learn," says Herbert S. Chase Jr., M.D., deputy dean for education.

In the past, students memorized anatomical features that they either would forget by the time they needed the information or never needed to know in the first place. "Given the myriad anatomical details, rather than examine every structure, we ask 'What does a physician who interacts with

human anatomy need to know?'" says Chase, adding that surgeons need to know the anatomy of operations they perform, radiologists need to know anatomy to identify abnormalities and disease and emergency physicians and anesthesiologists need to know anatomy to perform essential procedures.

Even more important is finding ways for students to retain what they've learned so they can apply it when treating patients. Accordingly, the new focus of the course is not on information, but on transformation—a change in the students' thinking process. No one learns a foreign language by memorizing a dictionary and rules of grammar; fluency occurs only when one begins to think in the new language, says Lawrence J. Rizzolo, PH.D., associate professor and course director. Similarly, students learn the language of medicine not by memorizing anatomical details, but by learning to think anatomically. "What we're trying to do is prepare students for lifelong learning," explains Rizzolo. "We're trying to give them the tools and skills so when they see new information they have a way to assimilate and acquire that information."

To achieve that goal, the course addresses four areas: clinical reasoning, visual reasoning, structure/function relationships and knowledge of anatomy. The tools used to achieve proficiency in those areas have been constructed to reinforce different skills and learning styles.

A clinical context

Dissection remains at the heart of the course, but it is now anchored in clinical medicine. Previously students studied structures in terms of their relationship to other structures. Now every dissection is a clinical case, and surgeons specializing in that day's procedure are brought in as guest instructors. Instead of telling his clinical colleagues what anatomy he wanted to teach and asking them to come up with clinical cases, Rizzolo was asking them to teach cases that students were likely to see, along with the anatomy behind those cases. It was a sea change in how anatomy courses have been organized. Using real surgical instruments, the students are practicing actual surgical procedures under the assumption that they will better retain information that they learn in a practical context.

While other medical schools use some surgical cases to teach anatomy, Yale is the only medical school in the country that uses surgery as the basis for the course for first-year students, according to Rizzolo, who sits on the educational affairs

committee of the AAA. Both students and faculty say the method works. “In a lot of anatomy programs you just dissect,” says student Judah D. Weathers. “Here we relate to disease and surgery.” Even mistakes offer moments of insight. “When you make one and understand it, you never forget it,” says Alicia Little. Instructors accustomed to the old system are already converts to the new approach. Shukrulla Ghofrany, M.D., a retired surgeon who has taught anatomy for the past four years, thought clinical cases would be confusing to students who have little knowledge of medicine. But feedback from students and his own observations have changed his mind. “I have to admit that I was totally wrong,” he says. Using a clinical outcome as the basis for teaching anatomy is bound to work, according to Chase. “If students can identify every important anatomical structure while doing a hysterectomy, then they know the relevant anatomy of the pelvis,” he says.

Another new aspect of the course is the expanded use of computers and the Internet. In the year-old anatomy labs at the Anlyan Center, each dissection table has its own workstation suspended from the ceiling. These computers are meant to be used during labs: the keyboards are made of soft rubber that is washable and virtually indestructible, and the course’s dissection manual, *Anatomy Clinic*, is distributed online. The manual, an interactive tutorial developed by Yale faculty, prods students with questions, and if they answer at least partially correctly, it supplies the full answer. If not, it directs them to resources with the correct information. Students can also access the Visible Human Dissector, a simulator based on the National Library of Medicine’s Visible Human Project and developed by researchers at the University of Colorado. This software allows students to view thousands of three-dimensional images of the human body in which each anatomical feature is color-coded and can be isolated, rotated, eliminated or viewed in cross section.

“We try and supply a variety of different learning modalities and teaching styles,” says William B. Stewart, PH.D., associate professor and chief of the Section of Anatomy and Experimental Surgery. “Some students love computers, others always look at the dissection, others always have their nose in the manual.” Some schools have abandoned cadavers in favor of virtual dissections done via computers. Encouraging that trend are the scarcity of cadavers as well as instructors, and, in part, scandals at Tulane University and the University of California, Los Angeles, where employees sold cadavers or

body parts to body-brokerage and research companies. But these computer programs haven’t been successful, because students need to learn in three dimensions. “It’s like having a map and directions,” says Frangos. “You can study it, but once you drive it, you never forget it.”

The tools of diagnostic imaging also help students visualize the inner workings of the human body. In the past, imaging was used intermittently, but in the new course it’s used during each lab. Groups of students gather around Michael K. O’Brien, M.D., PH.D., who is both an active surgeon and an anatomy professor. Using X-rays and CT and MR scans, students learn basic principles of radiology as well as the concepts of anatomy. O’Brien asks them to sketch structures and leads them to answers to their questions. Students say radiology allows them to make two-dimensional images three-dimensional, helping them visualize what may be difficult or too messy to see in the dissection lab.

Learning as a group

Under the Yale System of Medical Education, students are expected to be independent learners who seek out information and take responsibility for their education. Yale students tend to be highly motivated to study on their own, but Rizzolo has found that they learn anatomy better in small groups. For the past two years, students have formed “learning societies” of 20 students divided into four groups, with a mentor for each. Students prepare for class individually, then meet with their societies to explore unresolved questions. Individual students become experts in their assigned areas and, at conferences, pool information and teach their classmates. Each group explores the core principles of clinical anatomy by combining different perspectives on a problem.

Even lectures, one of the traditional pillars of the anatomy course, utilize group dynamics. Students often break into groups at the beginning of a lecture to take a test, first individually and then, following a discussion, as a group. Lectures often come after a dissection, a policy that some students find perplexing. But according to Rizzolo, “The documented reality is the lecture doesn’t make sense unless you struggle with the material first.” This year’s students will find that less time is spent in the lecture hall. “It’s a difficult transition going from receiver of information to seeker of information,” Stewart points out, but an important one for the students to make.

The anatomy course guides students through the process of acquiring information they will need. But it's also an introduction to death and dying, and the course strives to make students comfortable with these topics. For most students, Rizzolo says, the dissecting lab will be the first encounter with a dead person or the first observation of the ravages of disease. In a 2002 paper published in *The Anatomical Record*, he maintained that it is an ideal place to introduce concepts of humanistic care. "The lab evokes the students' memories, speculations, and fears about serious illness in themselves, their families, and loved ones," he wrote. He tells the class that to be able to help their future patients and their families, they have to confront their own emotions first. He encourages students not to suppress their emotions, but to express them freely, and not to be embarrassed in front of their peers or professors.

For the last several years students have channeled their feelings through a memorial service, called a service of gratitude. Those who participate spend about half a semester on the project, in which they express themselves through whatever means they choose, including poetry, music and art. In the anatomy hallway hang two contributions from past years: an intricate and beautiful drawing called *Handed*, by Brent Schultz '06, and a quilt assembled by the medical school Class of 2006 and the physician associate Class of 2004, with panels dedicated to each donor in the course.

State of the art

The anatomy course's new direction is largely due to Rizzolo's efforts to study and implement methods of teaching anatomy in a way that will allow students to recall information when they need it. A 10-day course for medical educators at the Harvard Macy Institute in Boston in 2003 was the genesis of a grant proposal to the Fund for the Improvement of Postsecondary Education (FIPSE), a program of the U.S. Department of Education. A \$400,000 grant to the anatomy program was approved and funded in 2003, and proposes a "modular, multimedia, multidimensional approach" to teaching anatomy from high school through college and clinical education. The course has been developed and used at the medical school since the fall of 2003, when students benefited from a pilot program that included some of the new features, such as interactive Web versions of sections of the dissection manual. This year it will be further refined before being rolled out to the physi-

cian associate and assistant programs at Yale and Quinnipiac University and the medical schools at UCLA, the University of Utah, the Mayo Clinic, the University of North Carolina and the University of Connecticut. "The FIPSE idea is a national solution to a national problem," says Rizzolo, referring to shrinking anatomy resources. "I think there are many schools that would want to do this," adds Chase, "but they need a blueprint and Larry and Bill are creating it."

William C. Rando, PH.D., director of the McDougal Graduate Teaching Center at Yale, surveyed last year's anatomy students to get their feedback and find out how they spent their time doing course work. "I was amazed at the overall positive response, but what was even more amazing was how easily students could articulate what it was about this course that was working for them," he told instructors at a faculty meeting at the beginning of the fall semester. Students said that dissection, conferences and computer-based learning played a major role in helping them learn anatomy. Students also said that the course offers more ways to learn and has helped them become more independent thinkers. "The way they learn anatomy is structured in a way that's more like how they work when they get on the floor—combining knowledge to solve problems and knowing where to go to get additional information," says Rando.

Meanwhile, Rizzolo has been studying the connection between Web-based activities and learning. Last year, he kept track of how much students used computer-based instruction and asked them to take an exam at the end of the course. On questions where Web activities had been available, he found that students who used them far outperformed those who didn't. If more Web activities were available (as they are in this year's course), those students may have scored much higher on the exam.

Redesigning the course has been a huge undertaking, one that is ongoing. Rizzolo asks faculty members to meet weekly to discuss what is or isn't working in the course, and find ways to improve and develop it. "What I'm most excited about is the reaction of the students when they hear what the course will be like," says Stewart, who wishes that he could have taken the course when he was a student. "I'm enthusiastic, but at the same time I'm a little jealous." **YM**

Jill Max is a writer in Connecticut.

Christian Northeast is an illustrator in Ontario, Canada.



How to save the life of a young driver

Doctors in states without graduated licensure can make a difference by insisting on restrictions.

“So we drove on toward death through the cooling twilight.”

—F. Scott Fitzgerald (*The Great Gatsby*)

Sixteen years as a teacher and practitioner of emergency medicine at Yale have taught me that there is no greater tragedy than the loss of a child, and no more difficult duty for a physician than to deliver unthinkable news to disbelieving parents.

Ironically, parents fear dangers unlikely to affect their children, such as kidnapping or murder, while neglecting a far greater menace: motor vehicle trauma. Car crashes are the leading cause of death for people ages 16 to 20, according to the National Highway Traffic Safety Administration (NHTSA), where I recently completed a two-year fellowship. The Centers for Disease Control and Prevention reported that 4,700 American teenagers died in cars in 2001. (By comparison, the number of child kidnappings ending in death is estimated at 100 annually.)

The teenage years usher in a period of dramatically increased risk of vehicular death and serious injury. A newly issued driver’s license may be seen as a ticket in a lottery of death and disability. The NHTSA reports that the fatality rates per million miles driven by 16-, 17- and 18-year-olds are 17, 13 and 7 deaths, respectively, far higher than the rate of 3 deaths per million miles for older drivers.

In view of these numbers, does it make any sense that most parents allow their newly licensed children to drive with few or no restrictions, and that some parents actually give children their own car at this age?

Traffic safety advocates oppose this laissez-faire approach and have persuaded states to enact legislation to protect new drivers. Known as graduated licensure, or GL, the laws impose restrictions on young novice drivers, gradually easing limitations over periods of three to 12 months. These restrictions, which vary by state, include a no-passenger rule, zero tolerance of alcohol and a ban on nighttime driving. For young drivers, these three factors are the major variables associated with high crash and fatality rates.

The effectiveness of GL is well-established. A 1996 study commissioned by the NHTSA found that GL reduced injury, fatality and moving-violation rates among 16- and 17-year-old drivers by about 20 percent.

So what can a parent do if his or her child is about to become a new driver in a state with no GL laws? This was what I experienced in Connecticut, which was not yet a GL state when my oldest son was licensed. First, after getting his learner’s permit, for over a year he had lots of practice with an adult at his side. When he got his license at 17, I imposed house rules including no passengers (except parents), no solo night driving and no “just driving around for fun” before age 18. Perhaps most important to the big picture, I used my position as president of the Connecticut College of Emergency Physicians to work with other groups to win passage of a GL

law, making all teen drivers in Connecticut safer.

Concerned parents living in states that do not have GL laws can and should take action. Educating state officials using information obtained from NHTSA and Insurance Institute for Highway Safety websites is a good start. Letters to the editor and the support of civic and school organizations are also essential. Finally, support from police is critical because of their role in enforcement.

The Emergency Department acts as a filter for illness and injury in the surrounding community. This gives emergency physicians the opportunity to identify seemingly random incidents and recognize patterns of pathology that call out for preventive measures. It would be short-sighted and, frankly, irresponsible to simply “treat and street” without going to the source of certain injury or illness patterns in an effort to reduce or eliminate them. There will be more heartbreaking moments of delivering unimaginable news to anguished parents. We owe it to ourselves and our children to do everything we can to make those moments as infrequent as possible.

Phillip A. Brewer, M.D., is an assistant professor of surgery (emergency medicine) at the School of Medicine.

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Andrew Hamilton

Noted chemist is named provost

Andrew Hamilton becomes second scientist named to Yale's top academic post.

Ask **ANDREW D. HAMILTON, PH.D.**, Yale's new provost, if it's an accident that both he and his immediate predecessor are scientists, and he chuckles. He points out that it took three centuries for the university to name its first scientist, Susan Hockfield, PH.D.—who left Yale to become president of the Massachusetts Institute of Technology in December—as provost.

"Two scientists in 300 years is not a flood," Hamilton said. "But, yes, I do think it represents a recognition by the institution that we need to place a very major focus on science, engineering and medicine in order to maintain Yale's place at the very top ranks of universities worldwide."

To that end Yale has embarked on a \$1 billion building and renovation project for facilities in science, engineering and medicine, both on the central campus and at the medical school. But that's only the beginning. "My hope is that we will be able to use these new buildings to attract some of the very best scientists in the world to ply their trade at Yale," Hamilton said. "At the same time, we must maintain those traditional strengths of Yale University, which reside in the humanities, the social sciences and the professional schools."

Hamilton joined the Yale faculty in 1997. He became chair of the chemistry department in 1999, where he is currently the Benjamin Silliman Professor of Chemistry. He was appointed deputy provost at Yale in 2003. Before coming to Yale he taught

at Princeton and at the University of Pittsburgh. A native of the United Kingdom, he was elected a Fellow of the Royal Society last May.

His studies of small molecules that influence biological processes have provided insights into drug design and cancer therapies. He has also studied neglected diseases such as malaria, Chagas disease and African sleeping sickness.

As provost, Hamilton is advancing President Richard C. Levin's vision of Yale's role in the world. Hamilton recently traveled to China with medical school faculty members to establish and cement relationships with Chinese scientists and universities.

Hamilton is also keeping his eye on relationships within the university. "I think there are many opportunities for collaboration in research between scientists and social scientists on this side of campus and researchers at the medical school," he said. "I hope, with my scientific background, to be able to further those connections."



Jaclyne Boyden



Robert Alpern



Roberta Hines



Margaret Hostetter

New finance officer crosses country to assume post at Yale

JACLYNE W. BOYDEN, a senior administrator at the University of California, San Francisco (UCSF), has been named deputy dean for finance and administration at the School of Medicine, effective November 1.

Boyden, who served as vice dean of administration and finance at the UCSF School of Medicine from 1992 until last year, has worked in academic medicine for more than 30 years, serving as associate dean at the State University of New York at Stony Brook from 1988 until 1992. At Yale, Boyden will oversee a financial operation that totaled more than \$750 million in income and expenditures for the year ending June 30, 2004. She comes to New Haven from a slightly larger, public institution with an operating budget of \$893.7 million in 2003.

"I am absolutely delighted to have Jackie join us in this new role," said Robert J. Alpern, M.D., dean of the medical school and Ensign Professor of Medicine. "She possesses strong financial skills and has gained considerable experience in her similar position at UCSF."

Boyden said her focus will be on supporting the school's three missions of research, education and clinical care and on helping to realize goals set by Alpern and President Richard C. Levin. "My job here will be to make sure there is an administrative infrastructure in place to support the missions and make improvements possible," she says. "On the financial side, there is seldom enough money to do everything that we might want to, but it will be my priority to ensure that the dean has accurate and reliable information so we are able to match resources with his strategic vision."

Three named to endowed professorships

The university named three members of the faculty at the medical school to endowed professorships in 2004.

ROBERT J. ALPERN, M.D., who became the 16th dean of the medical school in June, was named Ensign Professor of Medicine. Alpern came to Yale from the University of Texas Southwestern School of Medicine, where he was dean. He studied medicine at the University of Chicago and trained in internal medicine at Columbia University and in nephrology at the University of California, San Francisco.

ROBERTA L. HINES, M.D., HS '77, was named the Nicholas M. Greene Professor of Anesthesiology. She joined the faculty in 1982 and became chair of anesthesiology in 1995.

MARGARET K. HOSTETTER, M.D., was named the Jean McLean Wallace Professor of Pediatrics. She also serves as chair of pediatrics and is a professor of microbial pathogenesis. From 1998, when she joined the faculty, until 2002, when she was named department chair, she directed the Yale Child Health Research Center.



Charles Cha



Susan Hardy



John Persing



Marina Picciotto



Sally Shaywitz



Barry Zaret

Charles H. Cha, M.D., assistant professor of surgery (gastroenterology), has received a two-year, \$200,000 Dennis W. Jahnggen Career Development Scholars Award from the American Geriatrics Society. Cha will investigate the effects of aging on tumor angiogenesis and growth.

Gilbert H. Glaser, M.D., SC.D., professor emeritus of neurology, received honorary-member status in the American Neurological Association in October. The honor is awarded to those who have made unique contributions to neurology and neuroscience as investigator and teacher.

Roberto J. Groszmann, M.D., professor of medicine and director of the Section of Digestive Diseases at the VA Connecticut Healthcare System in West Haven, received the 2004 Ismar Boas medal from the German Society of Digestive and Metabolic Diseases in September in Leipzig, Germany.

Susan E. Hardy, M.D., FW '04, instructor in geriatric medicine, has received a 2004 Pfizer/AGS Foundation for Health in Aging Junior Faculty Scholars Award for Research on Health Outcomes in Geriatrics. Hardy will receive \$130,000 over two years to continue her research into transitions between disability and independence among community-dwelling older persons.

Janet B. Henrich, M.D., associate professor of medicine and of obstetrics, gynecology and reproductive sciences, received a 2004 Scholarship in Medical Education Award, in the category

of Scholarship of Integration, from the Society of General Internal Medicine.

Judith H. Lichtman, PH.D., M.P.H. '88, assistant professor of epidemiology in the Division of Chronic Disease Epidemiology, has received a three-year, nearly \$959,000 Health Protection Research Initiative grant from the Centers for Disease Control and Prevention for a study of the burden of cardiovascular disease in the elderly.

Albert C. Lo, M.D., PH.D., HS '01, assistant clinical professor of neurology, received a Presidential Early Career Award for Scientists and Engineers from the White House Office of Science and Technology Policy at a reception at the White House in September. Lo was honored for his contributions to new therapeutic strategies to restore function in people with multiple sclerosis.

Susan T. Mayne, PH.D., professor of epidemiology in the Division of Chronic Disease Epidemiology, was appointed to the nutrition subcommittee of the Food Advisory Committee of the Food and Drug Administration's Center for Food Safety and Applied Nutrition.

John A. Persing, M.D., professor of surgery (plastic) and neurosurgery, will begin his term as chair of the American Board of Plastic Surgery in May. Persing, who is just finishing his term as president of the American Association of Academic Chairmen in Plastic Surgery, has been chief of plastic surgery at Yale since 1992.

Marina R. Picciotto, PH.D., associate professor of psychiatry, pharmacology and neurobiology, has received a \$100,000 Independent Investigator Award from the National Alliance for Research on Schizophrenia and Depression for a project on new antidepressant targets in the brain. Picciotto will study the antidepressant effect of blocking the nicotinic acetylcholine receptor.

Teresa A. Ponn, M.D., assistant clinical professor of surgery, has been named associate director for breast surgery at the Yale-New Haven Breast Center. In a private practice in the New Haven area since 1985, Ponn has focused on caring for patients with breast malignancies.

A symposium in September honored the lifetime work of **Charles M. Radding, M.D.**, professor of genetics and molecular biophysics and biochemistry, who retired last fall. During his 37 years at Yale Radding focused his research on recombination, making major contributions to both theory and experimentation. Radding is a member of the National Academy of Sciences and an editor of the *Proceedings of the National Academy of Sciences*.

Sally E. Shaywitz, M.D., professor of pediatrics and a member of the Child Study Center, received the Townsend Harris Medal from her alma mater, the City College of New York, in November. The medal honors distinguished alumni.

Robert S. Sherwin, M.D., FW '74, the C.N.H. Long Professor of Internal Medicine, has received

the Long-Standing Achievement Award from the Novartis Pharmaceutical Corp. for his role in developing insulin pump therapy, a crucial advance in diabetes care. He received the award in September in Munich, Germany, at the 40th annual meeting of the European Association for the Study of Diabetes.

Stephen G. Waxman, PH.D., M.D., professor and chair of neurology, pharmacology and neurobiology, has been named the first recipient of the National Multiple Sclerosis Society's Stephen C. Reingold Award for 2004. The award recognizes the contributions of Stephen C. Reingold, PH.D., who, until his recent retirement, was responsible for the society's national research and training programs.

A symposium, "Advances in Cardiovascular Medicine and Surgery," was held in October to honor **Barry L. Zaret, M.D.**, the Robert W. Berliner Professor of Medicine, who stepped down last year as chief of the Section of Cardiovascular Medicine after 26 years.

Heping Zhang, PH.D., professor of public health (biostatistics), has received two grants totaling \$1.5 million over five years from the National Institute on Drug Abuse. He will use the grants to develop statistical methods for identifying candidate genes for nicotine dependence, drug use and psychiatric conditions.

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

The eternal triangle of a sound health system

A misfiled application steered Bill Kissick away from his dream job and into the world of health policy.

The ongoing drama of Bill Kissick's life involves a triangle, not of romance, but of health policy. The three sides of Kissick's triangle are access, quality and cost containment. "I can deliver any one of these three by compromising one or both of the other two," said Kissick.

William L. Kissick, M.D. '57, M.P.H. '59, DR.PH. '61, has been puzzling over his triangle's three sides since he began his professional life in Washington, in 1961. He was planning to start his

dream job at the National Institutes of Health (NIH), assisting in the lab of future Nobel laureate Baruch S. Blumberg, M.D. Thanks to a misfiled application, the young physician ended up not at the NIH, but at the office of the Surgeon General, where he was assigned to work on a health insurance plan for elderly Americans. With a further nudge from what he calls "The Princes of Serendip," Kissick became one of the authors of Medicare. In the 18 months that he worked on the program, Kissick got a crash course in the art of the possible from Wilbur J. Cohen, then assistant secretary of health, education and welfare.

By the time Kissick arrived in Washington, Cohen had survived almost three decades in government in administrations of various political persuasions, beginning with President Franklin Delano Roosevelt. Cohen, one of the architects of the New Deal, had proposed that it include national pensions and health insurance. The pensions came to pass when Roosevelt signed Social Security into law in 1935. "FDR dropped the health care idea, but Wilbur didn't," Kissick said. Thirty years later, after President Lyndon Johnson signed Medicare legislation, Cohen told the young physician, "If you choose to continue working in health policy, you must learn to appreciate delayed gratification."

His old mentor, were he alive, would be angered by the recent changes in Medicare, particularly the privatization of the program, said Kissick. He brands the new legislation entirely "political" and attributes it to the lobbying strength of the pharmaceutical and insurance industries. For

example, under the new legislation, Medicare will no longer use its enormous purchasing power to negotiate prescription drug prices. The lost savings further compromise Medicare's financial stability, Kissick said.

Not that Kissick—who is the George Seckel Pepper Professor Emeritus of Public Health and Preventive Medicine at the University of Pennsylvania School of Medicine, professor emeritus at the Wharton School and Penn's School of Nursing and visiting professor emeritus of health policy and management at the Yale School of Public Health—considers the original legislation he helped write to be perfect. As Kissick sees it, the drafters made three serious mistakes. They dramatically underestimated the growth of the elderly population and the sophistication of medical technologies that would become available in ensuing years. Perhaps most importantly, they did not count on rising patient expectations.

Those expectations are discussed at length in Kissick's *Medicine's Dilemmas: Infinite Needs Versus Finite Resources* (Yale University Press, 1994), currently in revision. "No society has sufficient resources to provide all the health services its population could utilize," Kissick explained. "We all expect the ultimate in health care."

In the 1970s Kissick took a sabbatical in the United Kingdom, where he had an eye-opening conversation with a man who was wearing a bilateral truss. Kissick advised him to have surgery for his hernia.

"I intend to," the Englishman answered. "I'm waiting."

"How long have you been waiting?" Kissick asked.

"Five years."

"That's appalling!"

"My neighbor has been waiting for six," the man replied.

The British system relies on citizens' willingness to wait. "Ignore the queue and the system collapses," said Kissick. He finds it unlikely that



ISABEL CHENOWETH

As they watched the signing of Medicare legislation in 1965, a mentor advised William Kissick that if he wished to continue working in health policy, he must learn to appreciate delayed gratification.

Americans would patiently wait years for surgery.

“Health care transcends the biomedical sciences. It’s a cultural affair,” Kissick said. In a vast and populous country like the United States, where it is difficult to define a single culture, he suggests that health care plans organized by states are more viable than a single-payer federal system.

But state-by-state health care is by no means a panacea, Kissick cautions. “The more I read, the more confused I get,” he said. But he is not giving up on the idea of a health policy that serves America well, despite his perplexing triangle. “By the time I finish the revision of my book, hopefully, I’ll have some idea,” he said. (He’s also counting on more than 150 physicians who have graduated from an M.B.A. program in health care management he and a Wharton colleague established there in 1968. “They are now challenged to address the issues,” Kissick said.)

Kissick’s model of perseverance is his wife, Priscilla, who in 1982 founded and directed the first Medicare-approved hospice program, which became part of the University of Pennsylvania Health System in 1998. The Kissicks met at a Yale tea when he was a medical student and she was at the School of Nursing. Kissick committed the social error of turning up at the refined white-glove affair run by faculty wives with several friends, all dressed in khakis and laughing and joking as if they were on their way to The Game. Spotting her future husband, Priscilla Dillingham remarked to a friend, “Somebody needs to straighten that guy out.”

The Kissicks, who have three sons and a daughter, recently celebrated their 48th wedding anniversary. According to Kissick, “She still hasn’t given up trying to straighten me out.”

—*Colleen Shaddox*

Hunting the secrets of the cell in San Francisco, and game fish across the globe

John D. Baxter, M.D. ’66, HS ’68, has an imposing presence. At 64, he is a tall, strongly built man with shaggy hair, an affable Kentucky drawl and a passion for the specialized hunt. As often as he can, he packs his gear and heads for Alaska, the Seychelles or the South Pacific to go fishing. He goes after marlin, tarpon, bonefish, trout, salmon and sailfish, and if you want to see him beam, ask him about the five world records he holds. But Baxter doesn’t go out with powerhouse rods and tackle; that would be too easy. No, he goes after the biggest fish in the sea with only a fly rod and delicate test line, tools requiring an artist’s touch.

“I love Alaska,” Baxter says, kicking back in his office at the University of California, San Francisco (UCSF), campus. “And I’m very passionate about my fishing.”

For the past three decades, Baxter has also passionately devoted himself to another specialized hunt: he has been trying to decipher the delicate mechanisms by which hormones, proteins and receptors interact inside our cells. Here, too, he has bagged some impressive trophies. In 1977, he, Peter H. Seeburg, Ph.D., Howard M. Goodman, Ph.D., and John Shine, Ph.D., were the first to isolate and clone the human growth gene. That led to the creation of the first synthetic drug to stimulate growth in children of short stature. It also led to drugs that increase milk production in dairy cows. Then Baxter and a UCSF research colleague, Robert J. Fletterick, Ph.D.,

became the first to reveal what a nuclear receptor looks like when it is binding to a hormone, a breakthrough that led to new structures in drug design. In 2003, in recognition of his pioneering research, Baxter was named to the National Academy of Sciences.

Now he believes he may be on to his biggest catch yet. Working with Thomas S. Scanlan, Ph.D., another colleague at UCSF, Baxter has developed GC-1, a new compound that is showing great promise in preventing and treating high cholesterol, heart attack and stroke. By working on multiple sites in the liver, GC-1 could prove far more effective in lowering cholesterol than the statins that most doctors prescribe today. Baxter says it also shows promise in reducing obesity and diabetes, especially the highly prevalent type 2 form.

“This compound is about 1,000 times more potent than the statins,” Baxter says. “It will not replace the statins. If it works out, it will probably be used in conjunction with the statins. It attacks a different part of the cholesterol pathway, so they’d work phenomenally well together.”

If GC-1 does fulfill its promise, it will crown for Baxter a lifelong quest. He was born and raised in Lexington, Ky., and did his undergraduate work at the University of Kentucky on an athletic scholarship, majoring in chemistry and graduating Phi Beta Kappa. When he entered Yale in 1962, it was quite a shock: “Even though I had a good education at Kentucky, I was not prepared for the Ivy League. I had a significant adjustment, adapting to the Eastern intellectual establishment. I

John Baxter has fished all over the world, and in his laboratory in San Francisco he explores the inner world of cells.



PHILIPPE LEUROX

thought my Kentucky accent was just fine, but that was not the prevailing view at Yale.”

Baxter struggled in his first two years, but then he found his legs, thanks in large measure to Philip K. Bondy, M.D., the head of endocrinology. “He was a wonderful mentor,” Baxter recalls. “By the time I graduated in 1966, Dr. Bondy was head of medicine. So I elected to stay on at Yale and do an internship and residency in internal medicine.”

Yale left a deep imprint on Baxter. “When I look back, the most wonderful thing about Yale was that it was patient. I struggled and Yale put up with me. And I’ll forever be indebted to Yale for that,” Baxter says. “And I could not have gotten better training. Once I got out and mingled with the guys who went to Harvard, Johns Hopkins, wherever, we guys who came out of Yale were quite competitive.”

After leaving Yale in 1968, Baxter joined the National Institutes of Health and began probing the inner workings of nuclear receptors. In 1970 he went west to UCSF, where his work on receptors led him into the field of human growth hormones. After he and his colleagues cloned the human growth gene, Baxter teamed with Fletterick to show how hormones bind to their thyroid receptor proteins. “That has had all kinds of implications for helping us design things that ultimately become pharmaceuticals. It has really paid off.” In 1979, Baxter was named chief of endocrinology at UCSF and director of the UCSF Metabolic Research Unit, and continues today to lead a team of researchers.

Baxter was among the first university researchers to create biotech startup companies. Not everyone approved. “At a time when interactions with industry were highly controversial in the university setting, John started biotech companies, several of which were very successful,” says Jan-Åke Gustafsson, PH.D., M.D., professor and chair of medical nutrition at the Karolinska Institute in Stockholm. “Although he received scorn from his academic colleagues, John kept working in new directions and thereby substantially contributed to modernizing the thinking in academia.”

Bert W. O’Malley, M.D., professor and chair of molecular and cellular biology at Baylor College of Medicine in Houston, says that even greater renown for Baxter may be in the offing. “Although GC-1 is not being tested on humans yet, it looks very promising,” O’Malley says. “It could rival or exceed the importance of John’s work with human growth hormone.”

In conversation, John Baxter comes across as a man fulfilled. For the past 40 years he has been married to Lee, his Kentucky sweetheart, and the couple has two grown daughters. Clearly, though, Baxter is a man who still dreams of sailing distant seas and hooking even bigger fish, and right now those dreams are riding on the wings of GC-1. “You go to medical school to be a doctor and make a difference. If this thing could ever work and not be bad for some unforeseen toxicity, that would be a very satisfying thing.”

—Paul Chutkow

Turning the tide of AIDS in New Haven, in a collaborative style

When Yale College turned him away as an applicant in 1961, it came as a shock to **Matthew F. Lopes Jr.**, M.P.H. ’77. He’d grown up at Yale, living at the Elizabethan Club on College Street, where his father was the steward. Lopes naively assumed that Yale, the only school he’d applied to, would accept him.

He applied again to Yale College after a stint as an Army cryptographer during the Vietnam War. After another rejection, he argued his case at the admissions office and ultimately was accepted.

Today, Lopes is the coordinator for AIDS services for the New Haven Health Department, where he oversees a staff of 17 who deliver education, outreach and care to New Haven’s HIV-positive community. He chose a career in public health after his plans to become a physician didn’t pan out. Nearing graduation from the combined M.D./M.P.H. program at the medical school in 1977, he had written his thesis on Reye syndrome, completed his course work for his M.P.H. and finished all but two semesters of medical school. After several attempts and near misses, however, he failed to pass his medical boards. He graduated from Yale with an M.P.H.

“The world doesn’t necessarily stop because you don’t get everything you want,” he said. “I’m living testimony to the fact that you can survive not passing your boards and still be involved in medicine or practice public health.”

Lopes had chosen the combined program because he wanted to practice

Matt Lopes grew up on the Yale campus and received bachelor's and master's degrees at the university. He still lives in New Haven, where he coordinates efforts to control HIV/AIDS.



ISABEL CHENOWETH

medicine in an urban environment and he felt he would need a public health background. As it turned out, public health was probably the better choice for him, because it gives him the opportunity to deliver health care to a larger segment of the population than he could were he in private medicine. “In public health we see a lot more people and have a better impact in some respects,” he said. “A lot of people with HIV/AIDS need primary care and supportive services, and we have the models to make it work.”

Lopes came to the city's health department after working as an epidemiology consultant at the state health department, a hospital administrative intern at the state's Department of Mental Health and a minority recruiter at the School of Public Health. He joined the city's AIDS division in 1993, about three years after the city initiated its groundbreaking needle exchange program. Lopes has kept the program going, sending a van out five days a week to sites around the city where people can exchange used syringes for new ones and receive support services such as drug treatment referrals and HIV counseling and testing. With intravenous drug users accounting for 48 percent of New Haven's AIDS cases, Lopes believes the program is essential to fighting the spread of HIV/AIDS. He shuffles resources to fund it, since federal support is not available. “We try to meet people where they are and bring them to where we want them to be, without being judgmental,” he said.

When Lopes joined the health department at the height of the AIDS epidemic, there were almost 280 new cases reported that year in New Haven;

today there are about 80. But there are 680 HIV/AIDS patients and their families in New Haven who receive care through the New Haven HIV/AIDS Case Management Consortium, and delivering that care can be complicated. Lopes, with the support of community-based organizations, has built an infrastructure with funds from the Ryan White CARE Act, a federal program designed to help provide care for HIV/AIDS patients and their families. He coordinates HIV/AIDS case management for the city of New Haven through another consortium of five community agencies (including the AIDS Interfaith Network and Hill Health Center), and oversees the health department's outreach and education efforts, HIV counseling and testing, and drug treatment referral. He is also the coordinator of the Mayor's Task Force on AIDS, whose mission is to foster community response to the HIV epidemic and raise awareness of AIDS at the local, state and federal levels. “We've built a huge network of collaboration,” he said, referring to the myriad agencies and officials involved in the fight against AIDS.

Although the number of new cases of HIV continues to decline, the Centers for Disease Control and Prevention estimates that 25 percent of those infected may not know they harbor the virus. Lopes sees his mission as finding those people and getting them tested and into treatment. To do that, he has looked at new ways of reaching people who are at risk, those who engage in intravenous drug use and unprotected sex. In an effort to address New Haven's needs, Lopes has introduced flex hours so that his staff can start and end their day later, when they have a better chance

of connecting with residents who need services; some of the agencies in the consortium have extended their hours as well. His department's outreach efforts include visiting drug sites, beauty parlors and even soccer fields on the weekends to help disseminate information, as well as running peer education groups with teens and going into schools to promote harm reduction. In addition, Lopes organizes community-level interventions, such as World AIDS Day, which took place at Center Church on the Green on December 1 last year.

At 61, Lopes shows no signs of slowing down, although retirement isn't far off. He and his wife, Evelyn, an artist, plan to retire to either Brazil or Costa Rica in about four years. Lopes is undaunted at the prospect of picking up and starting over in a foreign country; over the course of his lifetime he has learned Spanish, Portuguese, French, Japanese and German. “I'm nosy and I like languages,” he said, “so I could live anywhere.”

—Jill Max

Familiar Faces

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

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Gordon receives the Peter Parker Medal for years of service

MARTIN E. GORDON, M.D. '46, has taken on many roles in his varied career. Of late the semiretired gastroenterologist has chaired the board of trustees of the Harvey Cushing/John Hay Whitney Medical Library and has lured such prominent speakers as genome researcher J. Craig Venter, PH.D., and recent Nobelist Peter C. Agre, M.D., to the library board's annual lectureships.

In October, at a ceremony in the Medical Historical Library, Gordon received the Peter Parker Medal, named for the 19th-century Yale medical and divinity school alumnus who went to China as a medical missionary. The medal is awarded for outstanding contributions to medicine and the well-being of the School of Medicine.

"He has been a supporter of many parts of the medical school," said Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. "Probably his greatest contribution has been to this library. I can't think of a more appropriate recipient

than we have this year. Marty has been described as dynamic and charismatic and a fixture at the Yale School of Medicine, and one that we have been thrilled to have. He really exemplifies what we look for in training doctors to become leaders of medicine."

Gordon offered thanks to legendary physicians at the school of medicine, including Milton C. Winternitz, M.D., and Gerald Klatskin, M.D. "Their wisdom became applied lessons, amplified while sharing the angst and joy of the life of so many patients," Gordon said, before adding thanks to his wife, Evelyn, and his children and their spouses.

"I cannot fully express how the Yale School of Medicine has shaped my own life," he said, noting that the school and Parker shared the same mission—"promoting the health and advancing the welfare of others."

He has produced award-winning films such as *Microscopy: Tools of Biomedical Science*, as well as teaching tools, including the Global Disease Guide. He continues as a dean of the Academy of Judges for the International Health & Medical Media Awards Ceremony.

Three med school alumni elected to Institute of Medicine

Three alumni of the medical school were elected to the Institute of Medicine in October. They are:

FRANCINE M. BENES, PH.D. '72, M.D. '78, director of the Harvard Brain Tissue Resource Center at McLean Hospital in Belmont, Mass. The center is the largest resource for the collection and distribution of postmortem brains from people with movement disorders, dementias and major psychoses.

HOWARD K. KOH, M.D. '77, M.P.H., professor of health policy and management, Harvard School of Public Health, and former commissioner of public health for Massachusetts. Koh's areas of interest include early detection and prevention of skin cancer, policy aspects of tobacco control and cancer disparities in racial and ethnic minorities.

JAMES S. MARKS, M.P.H. '80, director of the National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention. Marks develops ways to reduce or prevent the consequences of tobacco use, obesity and diseases such as cancer, heart disease and diabetes.



TERRY DAGRADI

Dean Robert Alpern congratulated Martin Gordon on his receipt of the Peter Parker Medal as Gordon's wife, Evelyn, looked on.



William Hindle



Frederick Greene



Peter Krause



Alan Silken



Najaf Ahmad and Fraz Ahmed Ismat



Joyce Oen-Hsiao

1950s

William H. Hindle, M.D. '56, was honored in July by the Department of Obstetrics and Gynecology at the University of Southern California Keck School of Medicine with the naming of The William H. Hindle, M.D., Breast Diagnostic Center in Women's and Children's Hospital at the USC Medical Center-Los Angeles. Hindle founded the clinic and served as director for 12 years before becoming an emeritus professor in 2000.

1960s

Steven Jonas, M.D., M.P.H. '67, MS, has been named a fellow of the New York Academy of Sciences. Jonas, a professor of preventive medicine at the School of Medicine at Stony Brook University, has focused on preventive medicine, public health and health care delivery systems analysis and has authored, co-authored, edited and co-edited more than 20 books and published more than 135 papers in scientific journals.

1970s

Frederick L. Greene, M.D., HS '76, a surgical oncologist and chair of surgery at Carolinas Medical Center in Charlotte, N.C., was named chair of the Commission on Cancer of the American College of Surgeons (ACS) for 2004 to 2006 at the annual Clinical Congress of the ACS meeting in October in New Orleans. Greene has served for the last four years as the chair of the American Joint Committee on Cancer.

Peter J. Krause, M.D., HS '73, director of infectious disease at Connecticut Children's Medical Center, is one of three authors of a chapter on institutional responses to Lyme disease and companion infections in North America in *Emerging Illnesses and Society: Negotiating the Public Health Agenda*, published last year.

Judith Rodin, Ph.D., M.A.H. '79, former president of the University of Pennsylvania and the first woman to lead an Ivy League institution, has been named president of the Rockefeller Foundation. She is the first female president of the foundation, which does community development work on a global scale. Rodin was on the faculty at Yale for 22 years and served as dean of the graduate school and as provost.

Alan B. Silken, M.D. '74, HS '78, assistant clinical professor of pediatrics at Tufts University School of Medicine and director of pediatric neurology at Newton-Wellesley Hospital in Newton, Mass., is the author of "Long-Term Management of Seizure Disorders," a chapter in *Pediatrics*, a textbook published last fall by Elsevier Mosby. One of the textbook editors is also a Yale alumnus, **Thomas G. DeWitt, M.D.**, HS '80, the Carl Weihl Professor and director of the Division of General and Community Pediatrics and associate chair of education in the Department of Pediatrics, University of Cincinnati College of Medicine.

1980s

Guy L. Fish, M.D. '85, M.P.P.M. '94, of Cambridge, Mass., a senior consultant and director of Fletcher Spaght, has been elected to the Board of Overseers of Beth Israel Deaconess Medical Center. Fish specializes in health care policy, biotechnology and finance issues. Before joining Fletcher Spaght, he served as the vice president of business and international development at Collagenesis.

1990s

Jason R. Klenoff, M.D. '98, HS '03, an otolaryngologist at the Ear, Nose, and Throat Center in Stamford, Conn., and Serena Mayeri, J.D. '01, a Samuel I. Golieb fellow in legal history at the New York University School of Law, were married on July 27 in New York City. Klenoff is also a clinical instructor at the Yale School of Medicine and an attending physician at Stamford Hospital.

2000s

Najaf Ahmad, M.P.H. '02, a researcher and analyst for the Robert Wood Johnson Foundation, and Fraz Ahmed Ismat, M.D., were married on June 20 in Princeton, N.J. Ismat is a post-doctoral fellow in cardiology and attending cardiologist at Children's Hospital of Philadelphia, and an instructor in pediatrics at the University of Pennsylvania School of Medicine.

Megan C. Leaderer, M.P.H. '02, a manager of outcomes research at Pfizer with a focus on Alzheimer's disease and schizophrenia, and Cisco Del Valle, M.A., a

founding member of Springbok Capital Management, were married on August 21 in Battell Chapel. The couple lives in New York City.

Joyce Oen-Hsiao, M.D. '02, and her husband, Allen Hsiao, a pediatric emergency medicine physician, welcomed the birth of their first child, Timothy, on May 24. They live in Hamden, Conn., and she is a resident at the Hospital of Saint Raphael in New Haven. She writes that they would love to hear from friends (joyce.oen-hsiao@aya.yale.edu).

Ingrid E. Paulson, M.P.H. '04, and Alexander J. Pugh, a student at Columbia Law School in New York, were married in Pentwater, Mich., on July 24. They met while working in San Francisco and plan to live there after Pugh's graduation.

A 15-minute educational video produced by **Ilene Wong, M.D.** '04, is being used in multiple sites in South Africa to promote adherence to antiretroviral therapy. The video, which Wong produced while she was a medical student, emphasizes basic drug-taking concepts and advice on improving adherence. It has been translated into Zulu, and may also be used in Botswana and Namibia. It is available online through the Yale Medicine Thesis Digital Library (<http://ymtdl.med.yale.edu/>).

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TERRY DAGRADI (2)

At the White Coat Ceremony last August, Dean Robert Alpern greeted first-year David Gimbel.

Good doctors and great doctors

Dean Robert Alpern urges the Class of 2008 to practice medicine with humility, empathy and compassion.

Stitched through the threads of the physician's white coat are emblems of both power and responsibility, Robert J. Alpern, M.D., dean of the medical school, told the Class of 2008 in late August, as the new students gathered for the ceremony that marks the beginning of their medical education.

Each of the 100 first-year students—who come from 14 countries, 44 undergraduate institutions and previous endeavors in public health, scientific research, the performing arts and investment banking—can be proud to have won admission to a highly competitive medical school, Alpern said. But he urged them to temper that pride with a sense of duty. “Each

slot in a medical school is a precious resource to this country,” he said, advising students to use that resource wisely and to assume primary responsibility for their education under the Yale System. “We’re so confident that [you will] that we’re not going to give you grades for a few years.”

He encouraged his listeners to pursue paths to leadership positions in public policy, service, medical education and research and to use their time at Yale to “find out what separates a good doctor from a great doctor.”

While urging the first-years on to high achievement, his primary message was one of humility, empathy and compassion for patients. “You control something that is the most important possession of people, and that is their health,” the dean said. The most important question physicians will ask themselves is: “How would I feel if I were in the position of my patients?” The answer, Alpern said, should deter-

mine how a doctor runs a practice, including how long patients are kept waiting, when their phone calls are returned and what sort of respect they receive from their doctor.

“All people deserve your respect. ... Perhaps no one needs it more than a patient who is struggling to cope with an illness,” Alpern said. He cautioned against the desensitizing aspects of a physician's daily routine and urged students to remember that sickness “is not a daily event for your patients.”

Following the dean's remarks, students walked on stage one by one to be clothed in their white coats by senior faculty. The day was, as the dean said, a celebration of their “talent and hard work.”

But along with high praise, he sent the new class out with a gentle reminder: “As others look up to you, never look down on them.”

—Colleen Shaddox

Charisse Orme and Keri Oxley shared a laugh during the White Coat Ceremony.





JOHN CURTIS (2)

FAR LEFT Geordie Glass and Julie Guentner listened to the Commencement address by former Surgeon General Antonia Novello.

LEFT Before the ceremony began Bernadette Shaw got a hug from a well-wisher as Rebecca Schuman looked on.

Former surgeon general urges PA graduates to “look for a calling”

Antonia C. Novello, M.D., M.P.H., DR.PH., the first woman and first Hispanic to become surgeon general, offered congratulations and counseling and posed challenges to the 34 graduates of the Physician Associate Program at their Commencement in September.

“It has been said by the sociologist Robert Bellah that your work as a professional defines you as a human being,” said Novello, now the health commissioner for New York state. “First there is a job, where the goal is simply earning a living and supporting your family. Then there is a career, where you trace your progress through appointments and achievements. Then there is a calling, the ideal blending of activity and character that makes work inseparable from life.

I hope you are not just looking for a job. I hope you are not just building a career. I hope you are looking for a calling.”

The first of the challenges facing the new graduates, said Novello, is an increasingly diverse society, one that is aging, comes from all over the world and speaks a multitude of languages. Health care providers, she said, must understand all aspects of their patients’ lives. “Patients don’t care how much you know until they know how much you care.”

Access to health care was the second challenge she cited, pointing out that 45 million people in this country lack health insurance. “Don’t treat poor people as second-class citizens just because they may not have the same economic or educational advantages that you enjoy.” Again citing the diversity of the patient population and the 14 million Americans who lack proficiency in English, she said, “Medical

training has to address the biases that we bring to medical school.”

Domestic violence is another challenge. “Health care professionals will fail 95 percent of the time to identify victims of domestic violence,” she said.

The final, and most important, challenge, she said, is professionalism. “Can we health care professionals maintain the traditional humanistic qualities of medicine in an increasingly corporate structure?” she asked. “I think we can. To do that, take care of people. Become a voice for the disenfranchised. Use your voice. Have the courage to put patients first.”

—John Curtis

AUCTION RAISES MORE THAN \$26,000

Among the first fund-raising events of the 12th annual Hunger and Homelessness Auction in November was a flag football game pitting first-years against second-years. The game, played on a soggy Harkness Lawn under a light rain with temperatures in the 40s, featured faculty “ringers” on the second-year team—Dean Robert Alpern, Associate Professor Jack Hughes and Registrar Terri Tolson. At half-time, with the second-years leading 12-6, Alpern couldn’t help teasing the opposing side. “I’m a little disappointed in the admissions committee,” he joked. An anonymous first-year offered a rejoinder: “You better not come back on the field!” The second-year team won the game 28-12. The activities, including silent and live auctions, raised more than \$26,000 for several New Haven charities.

—J.C.



TERRY DAGRADI



Kyeen Mesesan

Kyeen Mesesan, an M.D./PH.D. student in the Division of Epidemiology of Microbial Diseases at the School of Public Health, received the Lee B. Lusted Student Prize for best student presentation at the 26th annual meeting of the Society for Medical Decision Making in Atlanta in October. Her abstract, "Predicting the Impact of a Partially Effective HIV Vaccine and Subsequent Risk Behavior Change on the HIV Epidemic in Developing Countries: A South African Example," was one of six delivered at the opening plenary session.



Lisa Gary

Three PH.D. candidates in the Division of Health Policy Administration at the School of Public Health have received grants to support their research. **Lisa Gary** has received a grant from the Nonprofit Sector Research Fund of the Aspen Institute to support her research on racial disparities in health care and the role of the non-profit sector in promoting more



Nicole Quon



Angela Snyder

equitable health care. **Nicole C. Quon** has received awards from the National Science Foundation and the Horowitz Foundation for Social Policy to support her research into decision making at the National Institutes of Health and the Food and Drug Administration. **Angela B. Snyder** has received a dissertation grant from the Department of Health and Human Services Substance Abuse and Mental Health Services Administration to pursue her research. Her thesis is titled *The Effect of Substance Abuse Treatment on Wages*.



Ranjit Bindra

Ranjit Bindra, a student in his fifth year of the M.D./PH.D. Program, has received the Marie Curie Award from the Radiation Research Society. The award recognizes the scholar-in-training who shows the highest potential for a successful career in radiation and hyperthermia research. The award-winner receives \$1,500 to attend the annual meeting and present research findings.



JOHN CURTIS

DOWN'S FELLOWS SHARE A WORLD OF KNOWLEDGE

Last summer, 17 students in medicine, nursing and public health traveled to Africa, Asia, the Middle East, the Caribbean and Latin America on research projects supported by the Downs International Health Student Travel Fellowship. In October they reported on their findings on topics including diabetes risk in Haiti and post-traumatic stress disorder among victims of chemical attacks in Iran. Three students made oral presentations. Medical student Jessica Beard described the mental health of children in a refugee camp in northwestern Kenya. Anna M. Beitin, a student in public health, reported on the genetic susceptibility of children in Zambia to malaria. And nursing student Catherine E. Virostko, on right in photo, discussed the beliefs and practices of traditional birth attendants in Kenya regarding HIV/AIDS.

—John Curtis

Henry Bicker Bruyn, M.D. '43, died on August 7 at his home in Kentfield, Calif., at the age of 86. During World War II, Bruyn served as a lieutenant commander in the U.S. Naval Reserve medical corps. Bruyn, a pediatrician, was the director of student health services at the University of California, Berkeley, from 1959 to 1972, and was also a clinical professor of medicine and pediatrics at the University of California, San Francisco, School of Medicine.

Daniel W. Elliott, M.D. '49, of Dayton, Ohio, died at home on August 1 at the age of 81. Elliott was a medical corpsman during World War II and a captain in the U.S. Air Force Reserve during the Korean War. After his surgical residency at Ohio State University in 1957, Elliott joined the faculty there as an assistant professor and became a full professor in 1963. He later became a professor of surgery at the University of Pittsburgh. In 1976 he helped found the medical school at Wright State University in Dayton, where he was chair of surgery.

Lawrence Z. Freedman, M.D., HS '48, died from a stroke on October 6 at his home in Chicago. He was 85. Freedman, a pioneer in forensic psychiatry who explored the causes of assassinations, terrorism and mass murder, held joint appointments in the Department of Psychiatry and the Law School between 1949 and 1960 at Yale, where he co-founded and chaired Yale's study unit in psychiatry and law. In the 1960s he served on the National Commission on the Causes and Prevention of Violence.

Robert C. Lange, PH.D., associate clinical professor of diagnostic radiology, died on October 6 in New Haven at the age of 69. Lange, an advocate for the protection of human subjects in research studies, was a pioneer in MRI technology. After receiving his doctorate from MIT in 1962 and working at the Monsanto Research Corp., he came to Yale in 1969. Until his retirement in 2000 he held a variety of posts, including technical director for the Section of Nuclear Medicine in the Department of Diagnostic Radiology and MRI physicist and clinical technical director for the Magnetic Resonance Imaging Research Center. He also chaired the Radiation Safety Committee and the Radioactive Drug Research Committee for Yale-New Haven Hospital. After his retirement he worked part time, as chair of one of the medical school's two Human Investigation Committees.

William Lee, M.D. '41, of Bath, Maine, died on July 19 at the age of 89. During World War II, Lee was a Navy doctor in the South Pacific, where he earned a battle star and unit citation. Lee, who spent 20 years in occupational medicine, was instrumental in founding the Constructive Workshops, a sheltered workplace for people with disabilities. For 14 years he directed the employees' health clinic at Hartford Hospital.

Darius G. Ornston Jr., M.D., HS '63, of Greenville, S.C., died on November 19, 2003, at the age of 69. Ornston came to Yale as a psychiatry resident in 1960 and by 1982 had become an associate clinical professor of psychiatry. In 1986 he moved to South Carolina, where he researched and translated the works of Sigmund Freud. He also authored a book, *Translating Freud*. Ornston was a longtime member of the Associates of the Harvey Cushing/John Hay Whitney Medical Library at Yale.

Alex Poljak, M.D., FW '96, M.P.H. '03, of Branford, Conn., died on July 3, at the age of 41, while biking with his wife and son on Block Island, R.I. Poljak was director of occupational medicine at Greenwich Hospital and a clinical instructor of internal medicine (occupational) at the School of Medicine. He also founded and served as chair and chief medical officer at MedLinx Interactive, a medical software company in New York City, and established two companies, Integrated Medical Systems and Occupational Health Solutions.

Jeffrey S. Schechner, M.D. '91, of Guilford, Conn., died on September 7 at the age of 39. Schechner, an associate professor of dermatology at the School of Medicine and director of the Dermatology Service at the VA Connecticut Healthcare System in West Haven, focused on vascular biology tissue engineering, and conducted research on blood vessels in the skin and human skin grafting.

Charles D. Spangler, PH.D. '42, died on July 5 at Holy Cross Hospital in Silver Spring, Md., of pneumonia after a stroke. As a commissioned officer for the U.S. Public Health Service, Spangler traveled the world designing water supply and sanitation systems until his retirement in 1968. He then worked as a project manager for the World Bank in the Far East and retired a second time in 1980. Spangler invented a simple, easy-to-repair hand water pump, and to keep it affordable, he refused to patent it. Spangler also taught environmental health through the Centers for Disease Control and Prevention.

Parker J. Staples II, M.D. '66, died at the age of 64 on September 23 at his home in Barrington, R.I. Staples had a private practice in allergy and immunology and was the medical director for Medicare Services in Rhode Island. He also did research for the National Institutes of Health and taught at the medical schools at the University of Rochester and Brown University.

SEND OBITUARY NOTICES TO

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Compleat Pediatricians disbanded

After 48 years, The Compleat Pediatricians have taken in their shingle. The discussion group, formed in 1957 [“A Running Conversation About Children,” Spring 1999] to give young doctors insight into the psychological and social factors affecting their patients, has called it a day.

The group was dealt a blow when founding member Albert J. Solnit, M.D., HS '52, of the Child Study Center, died in a car accident in 2002. Solnit had remained a guiding force while John E. Schowalter, M.D., HS '61, served as the group's consulting psychiatrist. Schowalter's retirement from the faculty last year precipitated the group's official end, but he said that the timing felt “natural” for other reasons. Most members had retired from practice, and for those who continue to see patients, years of case reviews and frank discussion had done their job. “I finally feel competent to help families with behavioral issues,” Richard L. Shelling, M.D., HS '59, said with a smile.

When the group started meeting in the 1950s, Shelling and his contemporaries knew how to fight childhood infectious diseases that were all but eradicated by immunizations but had not learned to give “anticipatory guidance,” advice about child development and matters as profound as death of a sibling and as commonplace as sleep disturbances. Weekly discussions led to a psychoanalytic understanding of the problems, and input from psychiatrists helped them help families resolve their issues.

While the original group has disbanded, physicians locally and nationally have embraced its ideas and its model.

Around the country the Maternal and Child Health Bureau of the Department of Health and Human Services funds “collaborative office rounds” on The Compleat Pediatricians model—discussions involving pediatricians, psychiatrists, psychologists and social workers—at 12 academic medical centers. And another group of pediatricians continues to meet at Yale.

For Shelling, teaching students in the office takes the place of the group's meetings. “I want them to learn something about well child care and anticipatory guidance, which can help parents understand normal behavior and hopefully help prevent misunderstandings between parents and their children,” he said.

—Colleen Shaddox



MAY 1955

Alumni Bulletin

The Codex Paneth

“One of the world's most famous medical manuscripts, the six hundred year old Codex Paneth, has been acquired by the Yale Medical Library. This rare, early medieval manuscript on velum measuring 23.5 by 33.7 cm., contains 1,378 pages. The numerous beautifully colored miniature initials illustrating medical scenes, the many representations of surgical instruments, and the rubrication in blue and red are by two different and unnamed artists, one a North Italian, the other probably a Bohemian artist of the early XIV century school. These illuminations give an insight to the medical and surgical procedures of the period. Many of the scalpels, saws, forceps and other instruments shown are amazingly modern in appearance and in some cases closely resemble surgical instruments in use today.”



FALL 1980

Yale Medicine

Minority High School Students Learn First Hand About Biomedical Research

“Nine students from New Haven area high schools participated this summer in a Minority High School Biomedical Research Program at the School of Medicine. They were among 200 minority students enrolled in a nationwide program sponsored by the Department of Health and Human Services, National Institutes of Health, which provides an opportunity to learn about biomedical research ... as apprentices in universities, health professional schools, hospitals and other research centers.

“The nine New Haven area students, who were selected from 50 applicants, worked as research apprentices to faculty in the Departments of Pharmacology, Diagnostic Radiology, Internal Medicine, Neurology, Human Genetics, Epidemiology and Public Health, and in the Child Study Center. Yvedt Matory, a fourth-year medical student, was coordinator of the program at Yale. At the end of the summer, Ms. Matory and the students submitted written reports summarizing their experiences in the program to the NIH. ...

“This was the first year for the NIH Program, which funded 200 students at a cost of \$400,000. Forty-five institutions in 21 states participated.”

YALE TEAM PROVIDES TSUNAMI RELIEF

Within five days of the December 26 tsunami that devastated coastal areas in South Asia, six doctors and a public health worker from the New Haven area were on their way to Sri Lanka. Led by Ramin Ahmadi, M.D., M.P.H. '97, an assistant clinical professor of medicine and founder of the Griffin Center for Health and Human Rights at Griffin Hospital in Derby, Conn., the team included Joanne Cossitt, director of the Griffin Center for Health and Human Rights; Padmini D. Ranasinghe, M.D., a resident at Griffin Hospital, and Anu Walaliyadda, M.D., a physician at the Hospital of Saint Raphael in New Haven, both from Sri Lanka; Monique A. Tello, M.D., a pediatrics fellow at Yale; Sherwin B. Nuland, M.D. '55, HS '61, clinical professor of surgery; and Majid Sadigh, M.D., associate clinical professor of medicine.

Nuland compared the disaster response to that of 9/11, when emergency rooms geared up for patients who never came. Most people, he said, were killed outright by the tsunami, and those with major injuries were already hospitalized by the time the team arrived. "The surgical patients I saw had been digging in the debris, looking for bodies," he said. Nuland debrided wounds and applied antibiotic ointments and dressings. His colleagues treated hundreds of patients with respiratory infections, diarrhea, dysentery, malaria and other diseases.

A major concern for survivors is post-traumatic stress disorder (PTSD). On their return on January 15, Ahmadi and Nuland began efforts to send mental health professionals to Sri Lanka to train local health care workers in the treatment of PTSD. Rather than medical care, Nuland said, "it is psychiatric care that is needed."



Monique Tello, a pediatrics fellow at Yale-New Haven Hospital, examines a young Sri Lankan girl at a church in Valachennai, Sri Lanka, on January 4.

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