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The Rev. Audrey Tinsley is the pastor of the Pentecostal Assembly Church of Deliverance in New Haven, a community health advisor and a diabetic. All these aspects of her life come together in one of the projects of the Yale-Griffin Prevention Research Center, which is working to reduce diabetes among African-Americans.

BACKGROUND

Low-fat cooking is key to preventing and managing diabetes, one of the messages from the Prevention Research Center.

Photographs by Gale Zucker

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Part of a national effort to create community health partnerships, a Yale center is working with New Haven churches to prevent diabetes and with suburban school nurses to stop teen smoking. The goal? Healthier communities invested in their own outcomes.

By Jennifer Kaylin

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Well-rested residents make fewer mistakes

"Recreating the Residency" by Peter Farley [Fall/Winter 2004] contains a large amount of palaver garnered from secondary sources. The grand jury found insufficient evidence to return an indictment of murder against the attending physician. Instead they indicted the system of graduate medical education.

Ms. Zion did not die from an overdose of cocaine. She died from hyperpyrexia—her last recorded temperature was 108 degrees.

The Accreditation Council for Graduate Medical Education rules governing residents' work hours are based on New York state regulations enacted in 1989. Yale will find, as have many programs in New York state, that eliminating sleep deprivation and chronic fatigue will improve the physical and mental health of young doctors and reduce medical errors in patient care.

Bertrand M. Bell, M.D., Distinguished University Professor, Professor of Medicine, Albert Einstein College of Medicine of Yeshiva University

The writer was chair of the commission now known as the Bell Commission, formed by New York state health commissioner David Axelrod, M.D., after Libby Zion's death to investigate issues surrounding patient care and the training of physicians in New York hospitals.

The cause of Libby Zion's death remains a subject of debate, and indeed, no consensus emerged among investigating agencies as to what went wrong. A jury in a civil trial split the blame for her death between Cornell Medical Center's New York Hospital and Zion herself. An autopsy found traces of cocaine in her nasal passages, but subsequent tests turned out negative. A grand jury blamed the death on inadequate care and numerous mistakes, including a mishandled diagnosis, made by unsupervised interns and residents. —Eds.

Zaccagnino to retire as CEO of YNHH

As this issue of *Yale Medicine* was being prepared, Joseph A. Zaccagnino, M.P.H. '70, president and CEO of Yale-New Haven Hospital (YNHH) and the Yale New Haven Health System since 1991, announced his retirement after 35 years at the hospital. He will retire effective September 30.

"My decision to retire was not an easy one, but it was made with the recognition that as time passes, the opportunities for new experiences and challenges as well as the flexibility to spend more time with family cannot be deferred indefinitely," Zaccagnino said in a statement at the end of May. "I plan to continue to actively serve in the health care sector as an advisor to senior management and governing boards, by lecturing at the graduate level more frequently than has been possible recently and by serving on additional corporate boards."

Zaccagnino began working at the hospital in 1970 under the mentorship of John D. Thompson, R.N., M.S., professor and director of the Program in Hospital Administration at the School of Public Health. By 1978, when he was 32, Zaccagnino had become executive vice president and chief operating officer of YNHH.

Over the next 27 years, under Zaccagnino's leadership, the medical school's primary teaching hospital grew into a health care system that operates three hospitals in Connecticut, has annual revenues of \$1.5 billion, has 1,500 acute care beds and serves one out of every five hospitalized patients in the state. At YNHH Zaccagnino also oversaw construction of the Children's Hospital and the renovation of adult patient care areas.

A search committee representing both the hospital and the health system is already at work seeking a successor, and a new CEO is expected to be named this summer.

yale medicine

Alumni Bulletin of the Yale University School of Medicine Summer 2005, Volume 39, No. 3

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Yale Medicine is distributed to alumni, faculty, students and friends of the School of Medicine, as well as leaders in Yale University alumni activities.

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

Postal permit held by Yale University, 155 Whitney Ave., New Haven, CT 06520

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Small answers to big questions

They say an ounce of prevention is worth a pound of cure, but changing unhealthy behaviors is not always a simple matter—as anyone who has tried to stop smoking or lose weight can tell you. It's that much more complicated when the goal is encouraging healthy choices for an entire community. The public health work of the Yale-Griffin Prevention Research Center, described by Jennifer Kaylin in this issue's cover story ("Promoting Health, From the Ground Up," page 24), is even more ambitious in that its goal is to help not just one community but a half-dozen New Haven-area towns. When you consider that Yale-Griffin is one of 28 such centers across the United States, you get a true idea of the scale and scope of the undertaking.

Nonetheless, the guiding principles of the projects are that the solutions to some national public health challenges are local, rather than global or grandiose, and that people will solve their own problems when aided by solid information derived from careful research. The community-academic partnership has already produced results: close to half the suburban high school students enrolled in the center's smoking cessation program quit cigarettes, and in New Haven a dozen churches have educated their parishioners about diabetes prevention through a partnership with Yale-Griffin.

The other feature article this summer ("The Silent Scourge of Development," page 18) looks at a public health crisis in Africa that evolved predictably but without restraint

over several decades and has affected hundreds of thousands of people. Here, too, the prevention of disease—in this case schistosomiasis spread by freshwater snails in the Senegal River—was a key goal championed by Yale researchers hired in the 1970s to evaluate the public health impact of dam construction. Unfortunately, their recommendations were ignored. Kohar Jones, M.D. '05, who wrote her medical school thesis on this topic after several trips to Senegal, does a skillful job of describing the economic and cultural backdrop to the crisis and telling a story that connects several generations of Yale scholars.

On a sad note, we received the news that the former managing editor of *Yale Medicine*, Marjorie B. Noyes, died on May 7. A 1953 graduate of the School of Art and Architecture, Noyes kept the magazine on the mark and on schedule from 1971 to 1986, according to former Editor and Deputy Dean Arthur Ebbert Jr., M.D., now a professor emeritus of medicine. "She was a very careful, very meticulous editor," says Ebbert. "We would discuss what we wanted to put in each issue, and then she made sure it all got done." Noyes' history of New Haven industry, co-edited with Preston Maynard, was published in January. This issue of *Yale Medicine* is dedicated to her memory.

Michael Fitzsosa
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SECOND OPINION BY SIDNEY HARRIS



Yale trauma training preps Navy corpsmen

In two-day workshops at Yale the Navy's independent duty corpsmen learn the basics of trauma care.

When the Navy submarine USS San Francisco struck an uncharted, undersea mountain in early January, responsibility for the dozens of injured sailors fell to James H. Akin, the vessel's medical corpsman. For 22 hours, Akin triaged the wounded—whose injuries ranged from bruises and pulled muscles to a fatal blow to the head—and put sailors and officers to work cleaning and irrigating lacerations until he could suture them.

As he stitched up the wounded, Akin's main concern was machinist's mate Joseph A. Ashley, who had struck his head during the impact. Akin immobilized Ashley, checked his airway, breathing and circulation, and inserted an IV. He showed other

sailors how to monitor Ashley's airway while he tended to other patients. As rescue vessels approached the stricken submarine, Navy doctors on ships and bases around the Pacific advised the medical corpsman by radio. But when the rescuers arrived, heavy seas made evacuations impossible. Ashley ultimately died of his injuries.

In March, Akin received a Meritorious Service Medal for his performance during the crisis. And he credited his ability to handle the medical emergency to the trauma training he received at Yale, under the direction of Reuven Rabinovici, M.D., professor of surgery and chief of the Section of Trauma, Surgical Critical Care and Surgical Emergencies.

For the past several years, Rabinovici has directed a course in the basics of trauma treatment for the Navy's independent duty corpsmen, or IDCs, given by trauma surgeons at Yale. It's part of the 56 weeks of training the corpsmen receive before they're assigned to sub-

marine duty and the care of crews of between 130 and 170 men.

"Their scope of practice is very narrow—primary care medicine for adult males, 20 to 45 years old," said Lt. Donald Harris, PA-C, clinical program manager at the Naval Operational Medicine Institute Detachment. The detachment is stationed 50 miles east of New Haven at the Naval Undersea Medical Institute (NUMI) at the Naval submarine base in Groton, Conn. (In May the base appeared on a Pentagon list of military facilities to be considered for closing.)

In addition to medical duties, the IDC monitors shipmates for exposure to radiation, practices preventive medicine and is responsible for environmental and occupational health. Corpsmen are also responsible for the mental health of the crew, not an unlikely concern in a cramped, self-contained environment that recycles its own air, converts sea water into drinking water and can stay underwater for as long as food supplies last—up to 65 days.

"They're the doctor, nurse, chaplain and psychologist," said Capt. Paul C. Kelleher, M.D., director of education at NUMI. Their emergency medical supplies and equipment, Kelleher said, roughly correspond to what is available on a paramedic's ambulance. And their



During their yearlong medical training, the Navy's independent duty corpsmen spend two days at Yale, where they learn the basics of trauma care. Among the Yale faculty teaching the corpsmen was trauma surgeon Lewis Kaplan.



JOHN CURTIS (2)

training at Yale covers different kinds of trauma, including blunt injuries as well as gunshot and stab wounds. One classroom scenario involves a wounded Navy SEAL coming on board for emergency treatment.

The sessions at Yale began three years ago when NUMI sought to enhance trauma training. Yale's in-house program that teaches residents advanced trauma life support was adapted for IDCs. "This program is less than what the doctor needs, but it's what the IDCs need," said Harris. As the first line of care, IDCs learn how to stabilize patients until they can be evacuated to definitive medical facilities.

The training starts with classroom sessions that cover the initial evaluation and resuscitation of a trauma patient. Then corpsmen move on to an animal lab to practice basic surgical techniques such as intravenous access, chest tube placement, opening a surgical airway and emergency amputations. "They are all basic lifesaving procedures that the IDC may need to perform on board," said Rabinovici.

The next day the IDCs attend interactive sessions with Yale trauma surgeons who pose real-life scenarios—such as a stab wound in the neck—and expect the IDCs to describe the appropriate treatment. The IDCs also rotate through clinical electives in surgery and anesthesia at Yale-New Haven Hospital.

The training made a difference for Akin when the USS San Francisco collided with the uncharted mountain 350 miles southeast of its base in Guam. According to Harris, the program manager in Groton, "he felt confident in his knowledge and management of the injuries to his crew because of the trauma training he received" from Yale surgeons.

Rabinovici said he was glad to learn that the training had paid off. "It is not that we *said* we could help—indeed, we did help. I feel very good about that."

—John Curtis

Drugmaker invests in New Haven facility and joint projects at Yale

Like many enterprises with international reach, Pfizer makes its corporate home in New York. But the company has deep roots in southeastern Connecticut, having built what was then the world's largest manufacturing plant for antibiotics in Groton in 1946. Today, more than 6,000 Pfizer scientists and personnel work in drug discovery in Groton and at the company's Global Research and Development headquarters in nearby New London.

With the April opening of the \$35 million New Haven Clinical Research Unit (CRU), a 50-bed dedicated facility for Phase I drug trials, Pfizer further strengthened its ties to Connecticut and added new luster to a three-year-old research alliance with Yale.

At the CRU, volunteers will participate in trials of potential medicines that have cleared several years of safety studies in the laboratory. Pfizer will collaborate with bioimaging experts at the School of Medicine, who will use positron emission tomography (PET) and other technologies to track the action of drugs in the human body, especially in the brain.

Diane K. Jorkasky, M.D., Pfizer's vice president of clinical pharmacology, said that the ability to draw on the expertise of Yale scientists figured heavily in the company's decision to locate the CRU in New Haven. But those collaborations are just one example of Pfizer's partnerships with Yale.

In 2003, the company established a fellowship in memory of the late Patricia S. Goldman-Rakic, Ph.D., a

renowned Yale neurobiologist, to support a graduate student in neuroscience in Yale's Combined Program in Biological and Biomedical Sciences. Through Pfizer Faculty Development grants, five assistant and associate professors in the School of Medicine have been granted up to \$50,000 worth of research time at the medical school's Magnetic Resonance Research Center. And in a new joint effort of Pfizer's Women Leaders Network and the medical school's Office for Women in Medicine, a female medical school faculty member will spend 12 weeks working alongside Pfizer researchers in Groton and New London each year.

"The relationship is one of win-win for Yale and Pfizer," said Jorkasky, "and the biggest winners will be the patients who will benefit from the science that the partnership explores."

—Peter Farley

For stem cell researcher, Connecticut's initiative offers a new avenue for progress

In her Yale laboratory in 2001, Diane S. Krause, M.D., Ph.D., surprised the scientific community with her discovery that adult stem cells taken from the bone marrow of mice can produce liver, lung, intestine and skin cells. To her dismay, her studies and similar findings have provided ammunition to opponents of embryonic stem cell research, who have used her results to argue that research with stem cells derived from human embryos is unnecessary. Speaking in January at a hearing of the Connecticut General Assembly, the associate professor of laboratory medicine and pathology said, "To close off this avenue of research based on the early promise of adult stem cells is to play the odds with people's lives." She called upon the legislature to support both adult and embryonic stem cell research in the state.

In May the state legislature did just that as it approved a bill to commit \$100 million to embryonic stem cell research over 10 years. At a ceremony in Farmington a few weeks later, with

Krause and medical school Dean Robert J. Alpern, M.D., looking on, Gov. M. Jodi Rell signed the bill into law. The bill's passage is expected to boost this research at Yale and the University of Connecticut. The legislation establishes a two-step process in which experts in both science and ethics review requests for funding.

Unlike adult stem cells, which have shown a limited ability to develop into other cells, embryonic stem cells can generate virtually any type of cell in the body. Biologists believe they have the potential to help treat diseases such as diabetes and Alzheimer's and to repair the spine, heart and other organs. Along with Alpern, Krause advised the General Assembly as it drafted legislation to make Connecticut a "safe haven" for embryonic stem cell research.

This field of study has been limited in the United States by guidelines established by President Bush that restrict federal funding exclusively to specific embryonic stem cell lines established prior to August 9, 2001. Supporters of the research contend that many of those pre-existing lines have been tainted by cells from other animals, such as mice, and that the limited number of lines hampers opportunities for study.

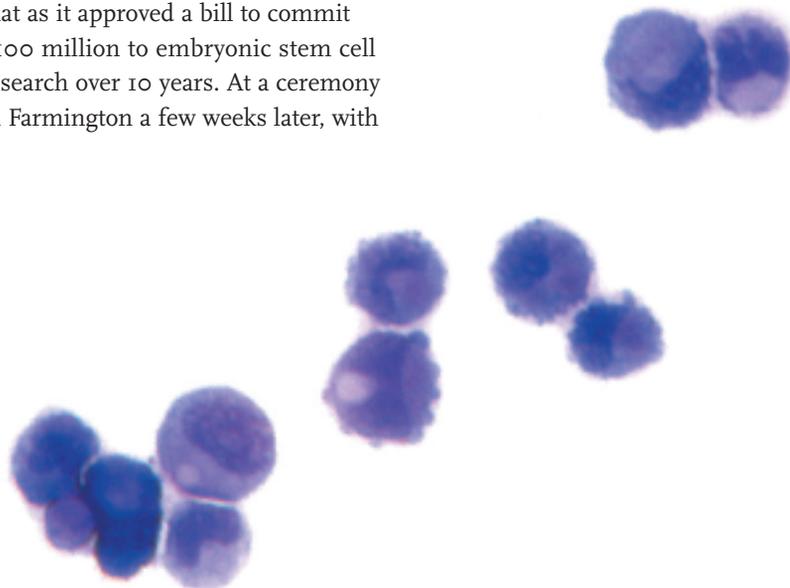
The controversial research received a major boost last year after California voters approved \$3 billion in funding for stem cell research over 10 years. New Jersey's acting governor, Richard J. Codey, announced in January that his state would invest an additional \$150 million in its stem cell institute, created in 2004 with \$11.5 million in startup funding.

In her Yale office, Krause pointed to an increasingly competitive research environment. "I've been contacted by states that have announced funding to see if I'd be willing to move," she said. "Connecticut doesn't want to lose the opportunity and researchers."

Krause is spearheading the effort to establish a stem cell program at Yale, and is one of more than 20 scientists across the university doing stem cell-related work. Recruitment of a senior leader for the Yale program began this past winter with an international search and will likely be followed by the recruitment of five to seven additional faculty members whose work is focused solely on stem cell biology.

Once established, the new program will likely have investigators performing both adult and embryonic stem cell research, with separate laboratories for any research using embryonic cell lines not approved for federal funding. "No one can predict," Krause said, "which lines of investigation will lead to development of effective and safe treatments. We can say with 100 percent certainty, though, that what we learn from embryonic stem cells will be useful for developing new therapies." Although she does not currently work with embryonic stem cells, she said, "I want the freedom to use embryonic stem cells as a tool when I need to use that tool."

—Marc Wortman



DIANE KRAUSE

Cells culled from mouse bone marrow differentiate into blood cells.

From the operating room to hospitals in need, REMEDY provides surgical supplies

In 1991, after several volunteer missions to Latin America, William H. Rosenblatt, M.D., HS '90, FW '91, professor of anesthesiology and surgery (otolaryngology) at the School of Medicine, made an observation that was to have far-reaching effects: many of the hospitals he visited were in dire need of medical supplies, while at Yale-New Haven Hospital (YNHH) many of those same supplies were discarded without being used.

Thus was born REMEDY (Recovered Medical Equipment for the Developing World), a nonprofit committed to recovering surplus medical supplies and teaching others how to do it.

What started as a local program at YNHH to collect opened but unused surgical supplies—which have never touched a patient but can't be reprocessed due to liability concerns—has grown into a grass-roots organization involving hundreds of hospitals around the United States. From Yale alone, the REMEDY program has donated

more than 30 tons of medical supplies to hospitals overseas. “Each of these pieces of material, whether it be a suture, a glove or a sponge, is going to wind up in another part of the world and be useful,” said Rosenblatt. The program has also saved the hospital over \$30,000 in disposal costs since its inception, at a cost of about \$200 per year for disinfecting and bagging the supplies.

Today, REMEDY trains hospitals to organize their own programs and has helped 358 hospitals begin recovery activities. The organization provides teaching packets free of charge, and with Yale's Office of International Health, has developed a notification program called AIRE-mail, in which medical supplies donated by hospitals and vendors are advertised via e-mail to 125 participating nonprofit humanitarian organizations. It has also developed a catalog called REMEDY Atlas, consisting of the 240 supplies most often recovered, which will help ensure that recipients are getting supplies they need.

Meanwhile, the collecting, sorting, packing and shipping of surplus medical supplies has largely been taken over by students. In 2001, RYSA (REMEDY at Yale Students Association) was started by Jonathan S. Cohen, PA '04, who is now a PA surgical resident at The Johns Hopkins Hospital.

“It's been incredible to see all this stuff come from what would have been the garbage in New Haven and end up being packaged and shipped all over the world,” said Cohen. Between last August and January, RYSA volunteers shipped 3,500 pounds of supplies from the New Haven area to eight countries.

For RYSA volunteers, long hours organizing medical supplies has its rewards. “The volunteers are having a direct effect with everything that they do,” said Rosenblatt.

—Jill Max

Alumni interested in starting a local REMEDY program may contact Silvia Botero at info@remedyinc.org.

et cetera ...

CIRA OPENS OFFICE IN INDIA

President Richard C. Levin inaugurated a new office for the Center for Interdisciplinary Research on AIDS (CIRA) in India in January. Joining him in the city of Chennai were CIRA's director, Michael H. Merson, M.D., and University Secretary Linda K. Lorimer, J.D. '77.

The new office will initially administer three projects. Project Parivartan, which is supported by a three-year grant from the Bill & Melinda Gates Foundation, will study community interventions designed to reduce HIV risk among sex workers, truckers and injection drug users.

A second project, supported by the Children's Investment Fund Foundation, will evaluate a model program that provides medical, psychosocial and nutrition services to families with a child infected with or affected by HIV/AIDS. The third project is a research and training program that will study the influence of religious and cultural factors on the mental health and transmission risk behavior of HIV-infected persons.

—John Curtis

CIS CONTRACT RENEWED

The National Cancer Institute (NCI) has renewed a five-year, \$5 million contract with the Yale Cancer Center to operate the NCI's Cancer Information Service (CIS) in New England. The cancer center has operated the New England service since it was created in 1976 to provide up-to-date cancer information to the American public. The CIS partners with state and regional organizations to develop education efforts for people lacking access to cancer information and services, provide current scientific information in understandable language and study ways to promote healthy behaviors.

“The CIS is a critical resource for the American public, and we feel privileged to be able to continue to provide this service,” said Linda Mowad, R.N., program director for the CIS at Yale.

The contract also includes a research component covering New England and seven other states to help the CIS educate the public about cancer and contribute to the nation's cancer control efforts.

—J.C.



Psychiatry, the law and the death penalty

For more than 30 years a Yale program has examined the interface of law and psychiatry.

Although death penalty decisions are always controversial, the case of convicted serial murderer Michael B. Ross has proven to be one of the most complex legal battles seen in Connecticut in recent years. Ross, who was found guilty of murdering six young women in the early 1980s, was sentenced to death 18 years ago. Since then, a series of appeals, hearings and overturned decisions has involved not only the courts but also two of Yale's forensic psychiatrists. Howard V. Zonana, M.D., professor of psychiatry, interviewed Ross before his 1987 trial, and Michael A. Norko, M.D., associate clinical professor of psychiatry, evaluated Ross in 1995, in 2004 and again in March when Ross attempted to waive his right to appeal. Norko found no evidence that Ross suffered from "death row syndrome" or that he was incompetent to waive his right to appeal. Ross was executed on Friday, May 13.

The Ross case is one of about 1,000 consultations for court cases both local and national that the Law and Psychiatry Division at the School of Medicine tackles each year. What began in 1973 as an elective for residents examining the interface between law and psychiatry has grown into a division of five units and 23 staff members that offers a one-year fellowship in forensic psychiatry, as well as courses for psychiatric residents.

"Forensic psychiatry is defined as the use of psychiatric expertise to aid in the resolution of legal problems, and it also deals with patients in settings like prisons, where there are special needs that have to be accounted for," explained Zonana, who directs the division.

That definition brings forensic psychiatrists into the courtroom as well as the clinic. They consult on everything from insanity defenses to the termination of parental rights. As part of their training, law and psychiatry fellows rotate through various settings: they work with law students in the Jerome N. Frank Legal Services Organization, they see the victim's perspective through postings with the state's attorney and they may work in the federal public defender's office or at the Connecticut Juvenile Training School run by the Department of Children and Families.

The division also contracts with the state of Connecticut to evaluate the competency of defendants in the New Haven region to stand trial—almost 200 cases a year. Under close faculty supervision, residents conduct evaluations, write reports and testify in court.

"We try to get them to approach each case from an objective, critical viewpoint, which may be different from the objective in clinical work, where you're trying to establish a rapport with the patient," said Norko. "In forensic psychiatry that's not necessarily the goal, because the outcome of your evaluation may or may not be helpful to the person."

On a broader scale, the division frequently examines legal issues such as a statute on the competency of



JIM FRAZIER

juveniles to stand trial or the legal regulation of psychiatry. "Psychiatry is the most legally regulated subspecialty in medicine because of the fact that we can detain people against their will," explained Zonana. The division also created a jail diversion project in 1995 that places a clinician in the court to assess defendants charged with drug-related misdemeanors and develop treatment plans as alternatives to incarceration. Thanks to the success of the project, the Connecticut legislature has since expanded it to all lower criminal state courts.

"It's a very diverse program, which I think is probably one of our biggest strengths," said Norko, who is the division's deputy training director. "The other is that we make a conscious effort to present more than one viewpoint about how forensic psychiatry should be done."

—Jill Max

Complex congenital heart patients live longer, need new treatment paradigm

“Sometime in the next decade,” said James C. Perry, M.D., professor of pediatrics (cardiology) and chief of the Section of Pediatric Cardiology, “there will be, for the first time, more people over 18 living with congenital heart disease than people under 18.”

Congenital heart disease (CHD), the most common of birth defects, affects 0.8 percent of all live births in any given year in the United States. Thanks to advances in surgical and medical management techniques for treating children born with structural abnormalities of the heart, many children for whom CHD would once have been an early death sentence can now expect to live well into adulthood.

That fact underlies the work of the Yale-New Haven Adult Congenital Heart Program, the first of its kind in Connecticut and one of only two dozen in the country. The outpatient clinic is staffed by Perry and coordinator Nicole K. Boramanand, A.P.R.N. '99, and the

program provides a collaborative and multidisciplinary approach to monitoring and treating adult survivors of pediatric CHD. The most common problems experienced by these patients are arrhythmias and heart failure.

“Pediatric heart patients in the past were often discharged from pediatric care based on age, but adult cardiologists are not usually trained to manage congenital heart disease. Those patients had nowhere to go,” Perry said. “Our program offers access to pediatric and adult cardiologists, heart failure specialists, pulmonologists, transplant specialists, specialists in high-risk obstetrics and other medical staff with essential expertise.”

Patient education is also critical. “Our focus is on preventive maintenance,” Boramanand said. “What treatments and lifestyle adjustments can increase the length and quality of life? For instance, we emphasize to our patients that the old notion that all people with adult CHD should avoid exercise is no longer accepted.”

Boramanand notes that another aspect of education and prevention is obtaining extensive diagnostic information up front. “If we get readings early and track them regularly, we can see situations that may require treatment.”

Perry points out that individuals who survive into adulthood with CHD also experience the full range of health concerns, from catching the flu to developing arthritis to managing pregnancy and childbirth, and notes that the center helps clinicians learn more about this population.

As of this spring the Yale-New Haven Adult Congenital Heart Program, which began in July of 2004, had seen nearly 100 patients ranging in age from 17 to their late 50s. “Life expectancies vary,” said Perry, “and this is a group of patients we are just beginning to learn about. But to see people with complex congenital heart defects going strong into middle age is remarkable.”

—Rhea Hirshman

et cetera ...

MOLECULE LINKED TO IMMUNE ATTACK

A Yale scientist has found that blocking a key molecule protects implants, pacemakers, artificial joints and other foreign biomaterials from attack by the immune system.

“Implantation of biomaterials, devices, and tissue-engineered constructs into tissues causes the development of a foreign-body reaction that can lead to implant failure,” said Themis R. Kyriakides, PH.D., assistant professor of pathology and biomedical engineering, a member of the interdepartmental program in Vascular Biology and Transplantation and lead author of a study published in December in *The American Journal of Pathology*.

Kyriakides and his team focused on areas where tissue and implants meet and foreign body giant cells form. In studies with mice, the team genetically eliminated the molecule, CC chemokine ligand 2 (CCL2), or blocked its action with decoy proteins.

The success of the experiments with mice opens up the possibility of finding targets for drugs to sustain implants.

—John Curtis

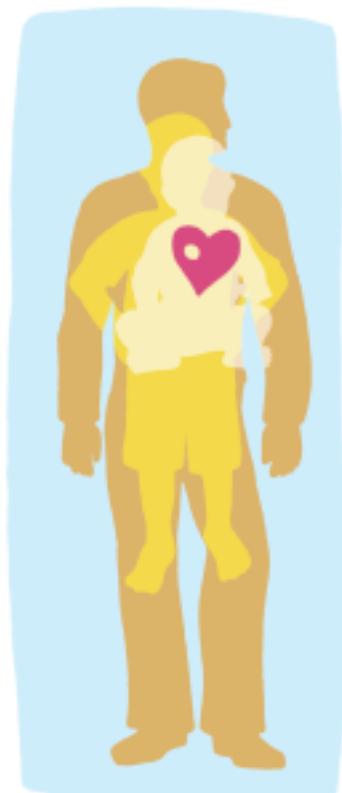
YALE TO LEAD STROKE STUDY

The School of Medicine will lead a \$33 million trial to examine a novel approach for preventing stroke—the Insulin Resistance Intervention after Stroke (IRIS) trial. Sponsored by the National Institute of Neurological Disorders and Stroke, the IRIS trial will test the effectiveness of reducing insulin resistance with pioglitazone, compared with placebo, for preventing recurrent stroke and myocardial infarction among nondiabetic stroke patients with a recent ischemic stroke and insulin resistance.

“This is the first trial that will look at the effect of this drug specifically to prevent clinically significant vascular events in nondiabetic patients,” said principal investigator Walter N. Kernan, M.D., associate professor of medicine.

Researchers at Yale designed the study and will coordinate its conduct at more than 60 research sites in the United States and Canada, recruiting more than 3,000 nondiabetic men and women over 45 who have insulin resistance and have had a recent ischemic stroke.

—J.C.



EINAT PELED

Prions found outside nervous system

Finding suggests more stringent monitoring of farm animals may be needed to protect the public.

Nancy H. Ruddle, PH.D. '68, the John Rodman Paul Professor of Epidemiology and Public Health and professor of immunobiology, is the first to admit that she's no expert on mad cows. Her laboratory studies the human lymphoid system and how it mediates chronic infection and autoimmune diseases such as diabetes and multiple sclerosis. But Ruddle's recent collaboration with pathologist Adriano Aguzzi, M.D., PH.D., in Switzerland has overturned one of the major tenets of public health efforts to curb mad cow disease.

More formally known as bovine spongiform encephalopathy (BSE), mad

cow disease is caused by prions—misfolded protein fragments that clump together and destroy the brain. Other animals, such as sheep, goats and mink, are also susceptible to prion diseases. In fact, researchers believe that the mad cow epidemic started because animal feed was contaminated with the brains of sheep infected with the prion disease scrapie. In humans, contraction of the variant Creutzfeldt-Jakob Disease has been attributed to eating BSE-infected beef—specifically, the animals' brain, spinal cord and immune system tissues such as the spleen and lymph nodes. Experts have assumed that other parts of the animal were safe to eat.

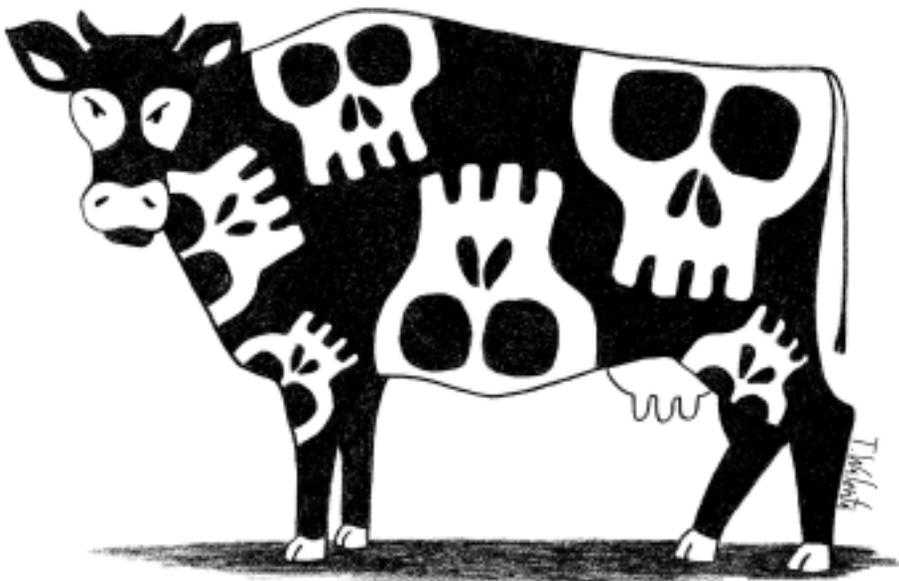
Aguzzi, a professor of neuropathology and molecular biology at the University of Zurich, has long been on the trail of prion diseases. In 1997 his team showed that the immune system's B cells, or B lymphocytes, which are

activated when the body mounts an immune response against common infections, may cause prions to replicate and spread. But no one knew how far.

Ruddle's team was working with mouse models of inflammation in the kidneys, pancreas and liver. Her work had shown that in chronic immune diseases, T and B cells can form outposts outside of the immune system that are very similar to lymph nodes. Since prion levels are known to be high in lymph nodes, the international team hypothesized that the organized outposts may allow spread of prions to other organs of the body beyond the nervous and immune systems. Sure enough, the researchers reported in January in the journal *Science* that when Ruddle's mice were infected with prions, their inflamed kidneys, pancreases and livers carried enormous prion levels—as high as those found in diseased spleens.

"It was thought that even if a cow was infected (with BSE), what was most important was that the brain didn't get into the feed. But if you have a chronic infection in that animal, you need to think about that, too," Ruddle said. The work may have far-reaching implications, such as the need for increased monitoring of farm animals, says Ruddle. Although cattle are routinely checked for fever, some inflammatory conditions such as early forms of diabetes, she notes, would not necessarily have visible symptoms.

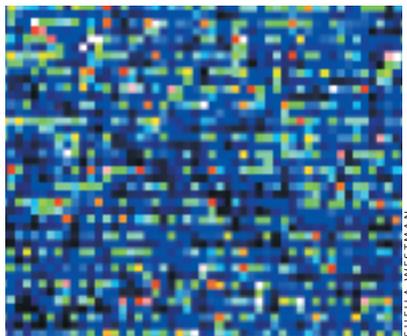
—Alla Katsnelson



Yale scientists find a genetic connection to age-related macular degeneration

Biomedical research into the genetic basis of disease has progressed at a rapid clip since the sequence of the human genome was announced in 2000, but this past March 10 saw the scientific equivalent of a triple play.

Three research teams, including one led by Josephine J. Hoh, PH.D., an assistant professor in Yale's Department of Epidemiology and Public Health, simultaneously announced that they had identified a gene variant associated with a greatly increased risk of age-related macular degenera-



On this genome map of a subject with age-related macular degeneration, red and white squares represent strong matches with probes that find gene variants.

tion (AMD), a progressive disease leading to blindness that affects more than 10 million elderly Americans.

The human genome can be thought of as a vast string of 3 billion letters in which each letter represents one of the four nucleotides that provide instructions to the body's protein-building machinery. The genome is 99.8 percent identical among humans, but after every 100- to 300-letter stretch on average are single nucleotide polymorphisms, or SNPs (pronounced "snips"), sites where one letter is substituted for another. Scientists believe that SNPs may help explain why some people are predisposed to certain diseases or respond differently to drug therapies.

Remarkably, all three of the teams who published their findings in March

independently zeroed in on precisely the same SNP, a spot on chromosome 1 that is home to a gene that codes for an immune system protein known as complement factor H (CFH). In its usual form, CFH acts as a brake on the complement system, a component of the body's innate immune response.

According to Hoh, whose group scanned the full genomes of 96 individuals with AMD and those of 50 controls, those who carry two copies of the newly identified variant in the CFH gene are nearly 7.5 times more likely than the rest of the population to develop AMD. "This is only an association," Hoh emphasized. "It doesn't really tell you that this is the cause of the disease."

Nonetheless, a faulty version of CFH may indeed be a culprit in AMD. For example, yellowish deposits at the back of the eye known as drusen, the clinical hallmark of AMD, contain complement proteins.

Hoh credits the Raymond and Beverly Sackler Fund for the Arts and Sciences for making the study possible. "This particular kind of study is expensive, not the normal thing a junior faculty member can perform," she said. "I am extremely grateful for the support from the Sackler Family."

Michael B. Bracken, M.P.H. '70, PH.D. '74, the Susan Dwight Bliss Professor of Epidemiology and Hoh's collaborator, adds that the work represents an entirely new way of doing epidemiology. "For the past 100 years, we've used a hypothesis-testing approach, where hypotheses were generated from animal studies or small human studies and then we did large epidemiology studies."

By contrast, whole-genome searches for SNPs are "hypothesis-free": "The association between a gene and disease is established first, and the biology is done after," Bracken said. "This takes all that we've thought about doing science and turns it on its head, and it's likely to have major payoffs in the future."

—Peter Farley

et cetera ...

MICRORNA LINKED TO ONCOGENE

A Yale scientist has identified a microRNA, *let-7*, that controls an oncogene implicated in about 20 percent of cancers, including lung cancer. The finding, reported in March in the journals *Cell* and *Developmental Cell*, presents new possibilities for diagnosis and treatment, according to Frank J. Slack, PH.D., assistant professor of molecular, cellular and developmental biology.

Oncogenes are segments of DNA that can induce uncontrolled cell growth and, ultimately, the formation of cancerous tumors. MicroRNAs regulate gene expression. *Let-7*, said Slack, stops the oncogene known as *Ras* from producing the Ras protein. In the absence of *let-7* RNA, cells in the nematode *C. elegans* continued to divide instead of differentiating normally. *Let-7* in humans, Slack said, is almost identical to the worm sequence.

Lung cancer has a poor prognosis, said Slack, "but gene therapy with *let-7* may be a way to alleviate it or slow it down."

—John Curtis

SMOKING TURNS RECEPTOR ON AND OFF

Cigarette smoking turns on and then inactivates brain receptors that are critical to the effectiveness of antidepressants, according to a study published by Yale scientists in *Biological Psychiatry* last fall.

Finding a way to manipulate those receptors could make antidepressants work more quickly—most now take up to three weeks to bring emotional relief. "This finding has implications for those patients who are depressed to the point of being suicidal and for the 30 percent of people who are not responsive to antidepressants that are now available," said Marina R. Picciotto, PH.D., associate professor of psychiatry, pharmacology and neurobiology, and senior author of the study.

The next step, Picciotto said, will be to study the role of these nicotine receptors, nAChRs, in regulating behavioral and cellular responses to antidepressants. The receptors may have a direct effect in mediating responses or they may act indirectly, by modulating neurotransmission in other cell types.

—J.C.

Pediatrician Robert Needlman spent two years revising and updating the classic *Dr. Spock's Baby and Child Care*. The eighth edition of the guide, the first revision since Benjamin Spock died in 1998, was published last year.



A radical notion of child rearing

Following in the footsteps of Dr. Spock, a Yale alumnus updates the classic guide for parents.

According to Robert D. Needlman, M.D. '85, Dr. Spock's *Baby and Child Care*—which has found a place on the bookshelves of 50 million parents across three generations—is “subversive.”

Benjamin M. Spock, M.D., MEd '29, initiated a revolution, said Needlman, with the first words of his 25-cent book, published in 1946. “Trust yourself,” Spock told parents. “You know more than you think you do.”

“Those famous lines were subversive to the doctor as expert,” says Needlman, who revised and expanded the book for its eighth edition, the first revision since Spock died in 1998 at age 94. In Spock's day, pediatricians dictated rigid schedules for sleeping and feeding and warned parents to resist the temptation to pick up fussy children for fear of spoiling them. Spock, in contrast, encouraged parents to discover what their children needed as individuals and to foster relationships of mutual affection and respect. This model of parenting is now so unexceptional that contemporary Americans may not appreciate how much of it originated with Spock. “We understand that it's no longer optimal, or even appropriate, to dictate to people what to do,” said Needlman.

An associate professor at Case Western Reserve University in Cleveland, Needlman incorporated his own insights in the new 992-page edition. He discusses gay and lesbian parents, how to stimulate a love of reading, how children respond to disaster and how young adults react when they leave home for college.

Needlman felt no qualms when he disagreed with Spock's recommendations. “I changed them—it was easy,” he said with a laugh. For instance, he eliminated the suggestion that a woman with postpartum blues cheer herself up by buying a new outfit. Instead, he suggests exercise, renewed contact with friends, talking to one's partner—and seeking medical help if the change of mood is severe.

The book combines the practical with the abstract, he said. “Some of it is very nuts-and-bolts: How do you change a diaper? A lot is philosophical: How do you raise children to be responsible citizens?” Needlman preserves Spock's exact words in short passages labeled “Classic Spock,” such



JANINE BENTIVEGNA

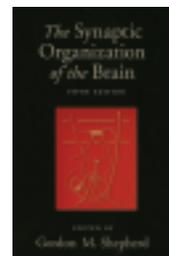
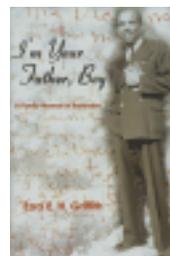
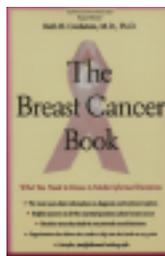
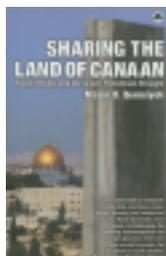
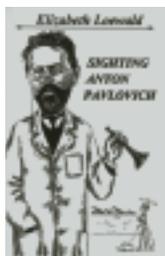
as Spock's views on TV: “There seems to be very little similarity between the world the electronic babysitter is selling to our children and the world we would like to see.”

Raised in Chicago in a household with the 1958 edition of Spock's book on the shelf, Needlman coincidentally followed Spock's career path. Both majored in English at Yale College. Both attended medical school at Yale, although Spock transferred to Columbia. After training in pediatrics at Boston University, Needlman took a job at Case Western in the same clinic where Spock had worked.

Needlman has found his own experience of the parent-child relationship endlessly interesting. He has a 16-year-old daughter, Grace, with his wife, Carol F. Farver, M.D. '85, a surgical pathologist he met on their first day at Yale medical school. As a father and a doctor, he has observed that children can be both predictable and surprising. “A wonderful mystery of parenting is that there are some qualities that show a lot of continuity. You can look at a child at two and then at 15 and say, ‘I recognize that.’ But there are a lot of things that you can't recognize: the same kid who was unhinged at five can be amazing, interested, interesting and capable of handling things beautifully at 15.” Six months after its publication by Pocket Books in June 2004, the Spock-Needlman edition of *Dr. Spock's Baby and Child Care* had sold nearly 100,000 copies. Not bad for a subversive little book that's been around since 1946.

—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.



Sighting Anton Pavlovich

by Elizabeth Loewald, M.D., FW '77 (Hermitage Publishers) The author considers Chekhov's life as a doctor and writer, describing how his chronic tuberculosis, interests and talents affected his character, life choices and literary work.

Preventive Cardiology:

A Practical Approach, 2nd ed.

edited by Nathan D. Wong, M.P.H. '85, PH.D. '87, Henry R. Black, M.D., FW '74, HS '75, and Julius M. Gardin, M.D. (McGraw-Hill Professional) This updated source provides clinically relevant information about the prevention of coronary heart disease, including risk factors and screening guidelines.

Radiology Illustrated: Gynecologic Imaging

by Seung Hyup Kim, M.D., Bruce L. McClennan, M.D., professor and chair of diagnostic radiology, and Eric K. Outwater, M.D. (W.B. Saunders) Over 3,000 images and brief descriptions of clinical disorders and diseases followed by case studies demonstrate the spectrum of benign and malignant gynecologic disorders and the optimal modality for imaging each condition.

Guide to Publishing a Scientific Paper

by Ann M. Körner, PH.D. '74 (Bioscript Press) This book explains how to produce, submit and revise a scientific paper for publication and offers advice about applying for funding.

Pathology & Genetics:

Tumours of the Breast and Female Genital Organs

edited by Fattaneh A. Tavassoli, M.D., professor of pathology, and Peter Devilee, PH.D. (Oxford University Press) This guide describes the pathology and genetics of each lesion, along with its epidemiology, etiology, clinical features, prognosis and predictive factors.

50 Signs of Mental Illness: A User-Friendly Alphabetical Guide to Psychiatric Symptoms and What You Should Know About Them

by James W. Hicks, M.D. '91, HS '95 (Yale University Press) From anger to sexual preoccupations, from cravings to obsessions, this volume describes the clues that may signal mental illness. Starting each topic with a vignette to illustrate a symptom, the author considers whether it arises from illness or constitutes a normal response to stress. The book outlines available treatments and coping strategies for each symptom.

Parent Management Training: Treatment for Oppositional, Aggressive, and Antisocial Behavior in Children and Adolescents

by Alan E. Kazdin, PH.D., director of the Child Study Center and the John M. Musser Professor of Psychology (Oxford University Press) This manual covers the background, principles and theory of parent management training and discusses techniques for treating children and adolescents who display oppositional, aggressive and antisocial behavior.

Sharing the Land of Canaan: Human Rights and the Israeli- Palestinian Struggle

by Mazin B. Qumsiyeh, PH.D., associate professor of genetics (Pluto Press) Qumsiyeh documents the core issues in the conflict between Israelis and Palestinians and articulates a road map for peace based on human rights and a shared future rather than apartheid.

American Dreaming and Other Stories

by Doris M. Iarovici, M.D. '92 (Novello Festival Press) The author explores the American ideal of success based on self-reliance and draws upon her own immigrant childhood to create stories of people in transition. She tells of their trials, resilience, empathy and hope.

The Breast Cancer Book: What You Need to Know to Make Informed Decisions

by Ruth H. Grobstein, M.D., PH.D. '57, FW '63 (Yale University Press) This guide provides the tools women and men facing breast cancer need to make informed decisions.

I'm Your Father, Boy: A Family Memoir of Barbados

by Ezra E.H. Griffith, M.D., professor of psychiatry and African American Studies (Hats Off Books) The author talks of father-son relationships, the cultural changes involved in moving to New York City in 1956 and the impact of modernization and globalization on his memories of his father.

A Field Guide to North Atlantic Wildlife: Mammals, Seabirds, Fish, and Other Sea Life

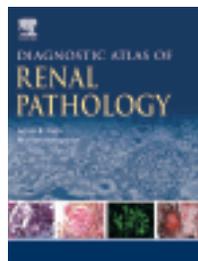
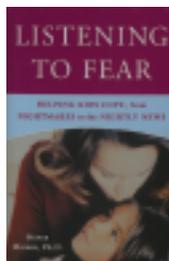
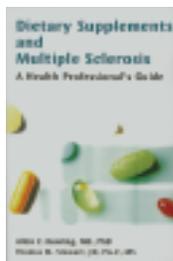
by Noble S. Proctor and Patrick J. Lynch, director of the MedMedia Group at the School of Medicine (Yale University Press) With range maps and text on pages directly opposite full-color illustrations, this guidebook provides concise information that facilitates quick identification of more than 200 species of wildlife on or near the Atlantic coast.

The Synaptic Organization of the Brain, 5th ed.

edited by Gordon M. Shepherd, M.D., PH.D., professor of neurobiology and neuroscience (Oxford University Press) This book covers new advances in the study of the neural basis of brain function resulting from the mouse and human genome projects, biochemical analyses and laser microscopy of dendrites. Each chapter highlights the principles common to all regions and the adaptations unique to each.

Carotenoids in Health and Disease

edited by Norman I. Krinsky, PH.D., Susan T. Mayne, PH.D., professor of epidemiology, and Helmut Sies, PH.D. (Marcel Dekker) Carotenoids such as beta carotene and lycopene are a focus of research on the relationship between plant nutrients and human health. This reference reviews studies on the latest biochemical research and reports findings regarding the use of carotenoids in preventing cancers and sunburn, as well as eye, heart, vascular and photosensitivity diseases.



Medical Physiology: A Cellular and Molecular Approach

by Walter F. Boron, M.D., PH.D., professor of cellular and molecular physiology, and Emile L. Boulpaep, M.D., professor of cellular and molecular physiology (W.B. Saunders) This textbook links molecular and cellular biology to the study of human physiology and disease and includes new material on hemostasis and fibrinolysis.

Health and the Income Inequality Hypothesis:

A Doctrine in Search of Data

by Nick Eberstadt and Sally L. Satel, M.D., HS '88, lecturer in psychiatry (AEI Press) While a number of recent studies suggest that inequality in income—not poverty *per se*—is bad for people's health, the rich included, this volume offers another view of this hypothesis. By controlling relevant variables, the authors suggest that income distribution is less a determinant of population health than the inequality hypothesis would suggest.

Dietary Supplements and Multiple Sclerosis:

A Health Professional's Guide

by Allen C. Bowling, M.D. '88, PH.D. '88, and Thomas M. Stewart, J.D., PA-C, M.S. (Demos Medical Publishing) Health professionals knowledgeable about complementary and alternative medicine can guide MS patients away from possibly harmful therapies and toward low-risk, possibly effective therapies. The supplements selected for inclusion are those with specific relevance to MS that are popular among the general public or known to have serious adverse effects.

Listening to Fear: Helping Kids Cope, from Nightmares to the Nightly News

by Steven Marans, M.S.W., PH.D., the Harris Associate Professor of Child Psychoanalysis in the Child Study Center (Owl Books) This text seeks to equip readers with hands-on tools: specific words and actions to elicit information and ease distress. The book is organized by age group, from infancy to adolescence.

Diagnostic Atlas of Renal Pathology

by Agnes B. Fogo, M.D., and Michael Kashgarian, M.D. '58, HS '63, professor of pathology and molecular, cellular and developmental biology (W.B. Saunders) This new atlas covers all major inflammatory, infectious, pre-neoplastic and neoplastic diseases of the kidney. More than 600 illustrations help readers to recognize the pathologic features and clinical manifestations of both common and rare renal disorders and to formulate confident and accurate diagnoses.

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

As the library enters cyberspace, patrons still arrive to read, write, research—and listen to music

Arthur E. Broadus, M.D., PH.D., Ensign Professor of Medicine, hesitates to advertise his not-so-private sanctuary: Yale's Medical Historical Library. He is hoping the crowds won't catch on.

"I escape over here for about an hour a day when I can, because it's peaceful and lovely and I can think and read, and sometimes write—and mostly get away from the din," said Broadus, section chief in endocrinology.

Down the hall and past the rotunda, in the Information Room of the Harvey Cushing/John Hay Whitney Medical Library, medical student Tejaswini More is studying from *Robbins Pathologic Basis of Disease* while listening to Haydn through earphones. The library computers have a really good music program, says More, and she gets more done here than in her room.

Just a few years ago, ophthalmology resident Amir Ahmadi, M.D., would have been a more typical library visitor: he has come to look up an article. But now Ahmadi is the exception, because patterns of library use have changed radically. Where annual electronic visits number in the millions, those who walk in the door just top 500,000, a ratio of 18 remote users for every person who walks in. And yet, said Director R. Kenny Marone, M.L.S., "Come in here in the afternoon, and you can't find a seat."

Medical students come to use the conference rooms for study groups, to seek guidance from a reference librarian or to borrow a laptop. Residents and students bring their personal digital assistants to a workstation in the Information Room, where they install applications such as InfoPOEMs, eMedicine and Griffith's 5-Minute Clinical Consult, which provide information about drugs and diagnoses. Students isolate themselves in carrels. Researchers read journals in the sun-drenched Morse Periodical Room. Downstairs, students click away in the Computer Resource Laboratory (CRL), night and day. "We used to have people leave at quarter of twelve, and they were unhappy," says Marone. "So we decided to make the CRL a 24-hour facility."

The library is also open to the general public. "They have access: It's Yale's way of giving back to the greater New Haven community," said Marone. Sometimes patients or parents drop in to look up information after a visit to the doctor or hospital.

When library service assistant George Moore began working at the library in 1978, "the furniture was dark, very heavy, very male, and there were heavy drapes on the windows. It was really a very forbidding place. Now we have carpeting, comfortable furniture, plants and better lighting. It's warm, it's alive. It's a very pleasant place to be—a livable space."

—Cathy Shufro



JEFFREY SACHS

The poor need help from the rich

You don't get much health care for \$4 per person. That's what India spends on public health each year, far too little to confront its growing AIDS crisis, said economist Jeffrey D. Sachs, PH.D., author of *The End of Poverty: Economic Possibilities for Our Time* and director of the Earth Institute at Columbia University.

India must increase health spending 10-fold, and to do so, Sachs argued at a February conference, "Health Crisis in South Asia," it needs help from the developed world. As its economy grows, India will be able to finance its own health system within a decade, but until then it requires assistance. That proposal is among the recommendations of the U.N.'s Millennium Project, directed by Sachs, a plan to meet the Millennium Development Goals, including halving the world's extreme poverty by 2015.

Sachs points out that in 2002, 22 donor countries including the United States promised to give 0.7 percent of their gross national product annually as development assistance to poor countries. The United States' rate is now only 0.15 percent.

"In many cases governments are ready to take action but need the donor countries to give the help they promised," said Sachs.

—Cathy Shufro



BILL McKIBBEN

Humans change their world, with no end in sight

Over the last 20 years writer Bill McKibben has looked at the ways humans have altered the world around them, and he has come away worried. "Without quite realizing it," he said at a talk in February sponsored by the Yale Divinity School and Yale's Interdisciplinary Bioethics Project, "we had grown so large that there was nothing except tectonic and volcanic forces that remained outside our deep influence. ... Humans have always interfered with the world around them, but their alterations have always had an edge. We live in a world where, all of a sudden, that is not true. There is no longer any edge to our effects on the world around us."

With the advent of genetic engineering, the influence of humans has turned inward and, McKibben said, it is important to draw a moral line. "I would say we draw it at germ line manipulation of human embryos, what a layman would call the creation of designer babies," said McKibben, author of *The End of Nature* and *Long Distance* and scholar-in-residence at Middlebury College. "It is a line that is very real and very palpable, yet allows room for human therapy."

—John Curtis



MARGRÉT ODDSDÓTTIR

Iceland's national health service provides for all

In Iceland, universal access to health care is enshrined in law. As a result the country has no private health insurance and the island's 290,000 residents rely on a national health service—state-run hospitals and primary health care centers—at minimal charge. If they see specialists in private practice, about 75 percent of the fees are reimbursed by the government.

Margrét Oddsdóttir, M.D., HS '92, professor and chief of surgery at Landspítali University Hospital in Reykjavik, described the Icelandic health system in March at the 50th annual Samuel Clark Harvey Lecture sponsored by the Department of Surgery. Most surgical procedures, she said, can be done in Iceland, but patients travel abroad for heart operations in infants, solid organ transplantation (other than living-related renal transplantation) and allogenic bone marrow transplantation. The national health system has a waiting list for surgery, but if waiting time exceeds six months, patients may travel abroad for treatment at government expense. Today, the only waiting list longer than six months is for cataract eye surgery.

Such a health system—which accounts for 10 percent of the country's gross domestic product—is possible in a small, homogeneous population, Oddsdóttir said, adding, "I don't know if it's possible in a large, heterogeneous population like the United States."

—J.C.



STEVEN MILES

Silence among doctors in the face of torture

Even as FBI agents and intelligence officers were warning their superiors that interrogations of detainees in Iraq and Afghanistan and at Guantanamo Bay in Cuba had gone terribly wrong, military doctors and nurses remained silent. "I have reviewed 14,000 pages of documents and can find only two instances of health care professionals trying to stop this abuse," said Steven H. Miles, M.D., director of the Center for Bioethics at the University of Minnesota, in a talk at medical grand rounds in March.

Those whose duty it was to see to the well-being of prisoners, he said, often failed: They provided inadequate health care. They supplied confidential medical data to interrogators and oversaw coercive interrogations. They filed false reports to cover up torture. And they failed to report abuses.

"I think we can look at the failure in two ways," Miles said. "There was a policy environment going down the chain of command authorizing the abuse. And there was a failure of accountability going up."

—J.C.

From the field of battle, an early strike at cancer

At the start of World War II, the U.S. government asked Yale to study chemical warfare agents. Building on research that had languished for years, two young scientists found in a derivative of mustard gas the first effective chemotherapy for cancer.

By John Curtis

NITROGEN MUSTARD THERAPY

Use of Methyl-Bis(2-Chloroethyl)amine Hydrochloride and Tri(2-Chloroethyl)amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders

LOUIS S. GOODMAN, M.B., Salt Lake City
 MAXWELL M. WINTROBE, M.D., Salt Lake City
 WILLIAM DANESHEB, M.D., Boston
 HORTON J. GOODMAN, M.B., Portland, Ore.
 MAJOR ALFRED GILMAN
 Medical Corps, Army of the United States
 and
 MARGARET T. McLENNAN, M.D., Salt Lake City

In a recent report the historical aspects of the use of β -chloroethyl amines (halogenated alkyl amines, nitrogen mustards) in the treatment of certain diseases of the blood-forming organs were presented and the chemical, pharmacologic, toxicologic and animal experimental aspects of these compounds reviewed.¹ The interested reader is referred to that report for orientation.

The present preliminary communication concerns the clinical use of halogenated alkyl amines in the treatment of lymphosarcoma, Hodgkin's disease, leukemia and a limited number of allied and miscellaneous disorders. In all 67 patients have been studied. These include 7 patients² treated by L. S. Goodman and Alfred Gilman at the New Haven Hospital; 34 patients treated by M. M. Wintrobe and Margaret T. McLennan at the Salt Lake County General Hospital; 16 patients treated by William Danesheb, Boston, and 10 patients treated by M. J. Goodman, Portland, Ore. The types of diseases treated are shown in the accompanying table. The youngest patient was 3 years of age and the oldest 76. The sexes were approximately equally represented in the series. Twenty-six of the 67 patients are still alive and under observation or therapy.

No attempt will be made at this time to analyze statistically the results obtained or to compare them with those observed after roentgen irradiation. The reasons for this are (1) the small number of patients in the series, (2) the prior use of radiation treatment for most patients, (3) the terminal nature and radiation refractory character of the disease in the majority of cases and (4) the small number of patients in the early stage of their disease. Rather, our purposes in this report are mainly to summarize briefly the clinical experiences obtained and to present the considered opinions of the various investigators concerned as to the status and the potential value of the β -chloroethyl amines in the syndromes enumerated. In subsequent more complete communications, comparison with the results of radiation therapy will be made and detailed hematologic and pathologic data will be presented.





NATIONAL LIBRARY OF MEDICINE (2)

Alfred Gilman and Louis Goodman (far left and left) had just published a pharmacology textbook when they were asked to study nitrogen mustard, a version of the sulfa mustard used in World War I gas attacks. In survivors the gas was found to destroy lymphatic tissue and bone marrow. The scientists believed it could also attack lymphoma. Their findings remained a military secret until 1946, when they were published in *The Journal of the American Medical Association*.

Early in 1942 two young assistant professors in Yale's new Department of Pharmacology, Louis S. Goodman, M.D., and Alfred Gilman, Ph.D., took on the study of nitrogen mustard. This agent was derived from a lethal gas used in the trenches of World War I, and the United States, which had just entered World War II, feared it might again be used in battle. By year's end, the two young scientists had found in an agent of death a medicine with lifesaving possibilities. Their use of nitrogen mustard with a human patient ushered in a new era of cancer treatment. "This was the first patient in the world treated by chemotherapy," said David S. Fischer, M.D., clinical professor of medicine, who gave a talk on the history of chemotherapy for the Beaumont Medical Club in March.

Scientists had been seeking a "magic bullet" for cancer since ancient times—the Romans practiced mastectomy, and Egyptians used topical preparations derived from medicinal herbs. By the 11th century the Arab physician Ibn Sina, known in the West as Avicenna, was using arsenical therapy systemically. The use of arsenicals in an effort to treat cancer continued for centuries, but without effect, said Fischer. "Until about 1900, the only real therapy for cancer was to cut it out," he said. "Cancer, by definition, was a surgical disease." Following Wilhelm Conrad Roentgen's discovery of the X-ray in 1895, medicine added radiation, which could shrink tumors, to its arsenal of cancer therapies.

After World War I, however, medical researchers noticed an interesting effect of mustard gas—it destroyed

lymphatic tissue and bone marrow. Perhaps, they reasoned, it could also kill cancer cells in the lymph nodes. But, Fischer said, this idea went nowhere. "They saw the relationship, but they didn't do anything about it."

Some experiments in this area continued and revealed that topical applications of nitrogen mustard, derived from the sulfa mustard used in battle, caused tumors in mice to regress. But that line of research also languished for a decade, until 1942, when the government's Office of Scientific Research and Development contracted with institutions around the country, including Yale, to study chemical warfare agents. Goodman and Gilman, who had recently published the first edition of what would become a classic text, *The Pharmacological Basis of Therapeutics*, began to study the effects of nitrogen mustard on lymphoma.

"They did their studies mainly in mice," Fischer said. "They found absolutely dramatic regression of the lymphoma." Further studies in rabbits were equally encouraging. Goodman, Gilman and their team decided it was time for a clinical trial. Gustaf E. Lindskog, M.D., an assistant professor of surgery, recommended a patient, J.D., a 48-year-old silversmith in the terminal stages of lymphosarcoma. Radiation no longer had any effect on his tumors.

"As his condition seemed hopeless, he was offered experimental therapy with nitrogen mustard," Fischer said. "In December of 1942, this 48-year-old patient was given 10 consecutive doses of nitrogen mustard, a 10th of a milligram to a milligram per kilogram of

body weight, roughly 2.5 times what became the standard dose. Nobody had any idea of what dose to give him." (The scientists had decided that there was a safe distance between a lethal dose and a therapeutic dose of nitrogen mustard.)

Within two days they noted a softening of the tumor masses. By the end of treatment the tumors disappeared. A month later, however, the patient relapsed, and subsequent courses of treatment were less effective. Nevertheless the scientists were encouraged. "This was proof," said Fischer, "that cancer could be treated by chemicals."

Further trials followed. Around the country, 67 patients, including seven at Yale, were treated with nitrogen mustard. The clinical trials remained a military secret, even from caregivers, until 1946—the first Yale patients' charts said only, "0.1 mg. per kg. compound X given intravenously."

By 1943 the team responsible for the first successful clinical trial of chemotherapy had disbanded. Goodman continued his research in Salt Lake City. Gilman entered the Army. Lindskog went on to become chair of surgery at Yale. But they had made a major contribution to cancer therapy by proving the worth of nitrogen mustard. Scientists began to look at other alkylating agents—which can attack cells at any point in their life cycle. And nitrogen mustard, which was incorporated into multidrug chemotherapy for Hodgkin's disease, remains a potent agent against cancer today.

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

“The silent scourge of development”

The Diama dam in Senegal was built to bring progress to the West African country. Instead, it brought schistosomiasis, an insidious but preventable parasitic disease.

In the Senegalese village of Mbagam, health worker Fatou Kine Manga fines those who enter the waters of the Senegal River. Despite her warnings to others, Manga admits to breaking her own rule. “Even me, I go to the river!”

Snails that carry parasites lurk there, threatening infection with schistosomiasis. This debilitating chronic disease attacks the poorest of the poor—those who, like Manga, lack access to clean water and sanitation and rely on infected water for drinking, cooking, cleaning and bathing. Poverty and schistosomiasis are rampant in Mbagam, both despite and because of the dams along the Senegal River.

I arrived in the West African nation of Senegal in September 1998, on my 21st birthday, to examine the health effects of the dams for my senior essay at Yale. This research would later become the topic of my medical school thesis, as well. For two months I lived in the capital city of Dakar,

the westernmost point of Africa. Described by a friend as a miniature version of Paris—after a bombing—downtown Dakar had multistory apartments with ornate wrought-iron railings and crumbling facades. Outside the skyscraper that housed the West African Bank, I dropped change on the blankets of beggars with polio. At the West African Research Center, as part of my study abroad program, I studied the country’s economics, politics and culture.

For my monthlong field project, my instructor in the indigenous language of Wolof encouraged me to follow in a Yale tradition and study schistosomiasis along the Senegal River. Twenty-one years earlier, he proudly told me, he had been the interpreter for a Yale team studying the potential effects of the dams on human disease. Wilbur G. Downs, M.D., M.P.H., led the team, which included Herbert S. Sacks, M.D., HS ’53; George A. Silver, M.D., M.P.H.;

More than two decades ago Yale public health experts warned that dams along the Senegal River would bring disease. A Yale medical student's research finds that their predictions have come true.

Article and photographs by
Kohar Jones, M.D. '05

A letter from Senegal.

Eric W. Mood, M.P.H. '43; Robert B. Tesh, M.D.; and Curtis L. Patton, Ph.D. My Wolof teacher's enthusiasm sparked my own. When the director of the nongovernmental organization Environment and Development Action in the Third World asked me to conduct an informal field survey on whether schistosomiasis would limit the socioeconomic development of the Senegal River region, I gladly agreed.

Sugar fields, rice paddies and near-desert

That November, I left the city for the Sahel, the region south of the Sahara, to begin my survey. Two months after the rainy season, the Sahel was already tan and dry. Herders wearing the traditional wraparound headdresses of the Pulaar people drove thin cattle over the land. Barbed wire prevented the herds from encroaching on the irrigated plots that nurtured dreams of agricultural development.

From the sugar cane boomtown of Richard Toll I continued a few kilometers downstream to Mbagam, a rice-farming village. My hosts were a prosperous farming family, wealthy enough to own a latrine and a mosquito net for guests. There was no electricity, but at night we gathered with villagers in a neighboring compound to watch television—powered by wires connected to a car battery—under the stars on a dirt floor next to cows. A relative of these neighbors lived in France, where he washed dishes and sent his wages home to support the family, pay the taxes and buy the car that provided power for the flickering images that allowed the villagers to dream of a different life.

The dams along the Senegal River also fed hopes of a new life. Omar Niang, president of the village farming cooperative, praised the dams for doubling the rice harvest. But standing next to a pump that transported water from



In 1998 author Kohar Jones, then a senior at Yale College, traveled to Senegal to investigate the links between dams and the spread of schistosomiasis.



the river to the rice paddies, he noted the negative aspects. Workers wore uncomfortable plastic boots for protection from infected water, and they all took the anti-schistosome drug praziquantel. “Everything has a good side and a bad,” he said.

Schistosomiasis, named “the silent scourge of development” by the World Health Organization in 1998, is the bad side of dams. It follows water development projects that create the perfect habitat for the snails that carry the disease (See sidebar, p. 21).

In 1994, less than 10 years after the dams were completed, Mbagam had a disease prevalence of 91 percent. About 2,500 villagers joined the estimated 200 million people worldwide who are infected with schistosomiasis. The other 9 percent joined 400 million people around the world at risk of infection.

The dams and the disease they brought emerged from Senegal’s colonial legacy. Senegal, the former jewel in the crown of colonial French West Africa, became independent in 1960 but maintained close trading ties with France. In 1968, however, France stopped subsidizing the dominant peanut economy just as a drought hit sub-Saharan Senegal. Both peanut farmers and nomadic herders saw their economies and lives devastated. Villagers flooded the capital cities in search of work, and starving masses threatened to

undermine political stability. In 1972, amid widespread famine, Senegal adopted French colonial plans to dam and irrigate land along the Senegal River.

With its neighbors Mali and Mauritania, Senegal formed the Senegal River Development Organization (Organisation pour la Mise en Valeur du fleuve Sénégal—OMVS). Dams provided hope for a desperate population. The massive hydroelectric Manantali Dam in Mali promised both electricity and a link between landlocked Mali and Atlantic trade routes. The small Diama Dam at the mouth of the river, between Senegal and Mauritania, would prevent salt water from creeping up the river bed during the dry season, allowing for two harvests of rice each year. Unfortunately, reality never matched the hopes.

By 1988 the dams were completed, but the promised new civilization never came to be. Following the dictates of Structural Adjustment Programs (SAPS) of the World Bank and International Monetary Fund, which demanded a balanced budget, Senegal dismantled and privatized its national health system and agricultural agencies just as they were needed most. Senegalese economists wryly renamed the SAPS “the Suffering of the African People.”

Disease comes to Richard Toll

During my month surveying schistosomiasis, my base was in Richard Toll, home to the Senegal Sugar Company (Compagnie Sucrière Sénégalaise—CSS). My new home became the gated Cité Cadre, where electricity generated by the burning of sugar cane stalks powered the air conditioners of the expatriate and Senegalese managers of the CSS, who directed development in the region. It was a city on a hill, separated from the center of town by a scattering of neighborhoods and the tall green waving stalks of irrigated sugar cane.

Trucks carrying molasses and sugar cubes to Dakar rumbled along the paved, two-lane National Route, dodging horse-drawn carriages, pedestrians and the occasional cow. The paychecks of the sugar cane workers supported a bustling market, a regional economic magnet. Electric lines strung overhead connected cement block homes. Two water towers were under construction. A *latrinisation* program promised to sanitize the town. Richard Toll was the model of agroindustrial development for the nation.

Without clean water and sanitation, the river becomes kitchen, laundry and bathroom, promoting an ongoing cycle of infection and reinfection.



A disease of poverty and progress

No disease is as clearly linked with development as schistosomiasis. Nicknamed the “germ of progress” in the 1970s for its close association with water development projects that allowed freshwater snails to thrive, schistosomiasis remains the “silent scourge of development.” Though preventable and treatable, it flourishes throughout the developing world. It has infected 200 million people worldwide, and threatens an additional 400 million, primarily in Africa, Asia and Latin America. Of those infected, 120 million people are symptomatic, 20 million have severe complications and 200,000 die each year, more than the number of deaths from AIDS, diabetes, kidney disease, pneumonia and influenza combined in the United States.

Humans are at risk when they enter freshwater sources infested with snails that release fork-tailed parasites called cercariae. Cercariae burrow through skin and grow into worms that inhabit the capillaries of the intestines or bladder. The worms mate and lay barb-tailed eggs that cut through vessel walls, eventually leaving the body in the feces or urine. When people relieve themselves near snail-infested water, the eggs enter the water and hatch, then grow into parasites called miracidia that lodge in the shells of specific snail hosts. Each miracidium gives rise to thousands of cercariae, and the cycle explodes.

An initial acute infection with schistosomiasis is followed by chronic debilitating disease. After an initial itchy rash at the site of cercaria entrance, accompanied by fever, weeks go by with minimal symptoms. The cercariae grow into worms that use molecular mimicry to evade detection by the immune system. Schistosome eggs, not the

worms, bring disease. Anemia—often severe, sometimes deadly—accompanies blood loss in diarrhea or urine. In many regions with endemic urinary schistosomiasis, a boy is considered to be a man after blood appears in his urine, thought to be a form of male menstruation.

Severe complications ensue when excess eggs wash deeper into the body, eliciting an inflammatory immune response. Liver scarring clogs the return of blood to the heart. Initial heavy infection with intestinal schistosomiasis can kill with bloody diarrhea, or cause irreversible paralysis if eggs are washed into the spinal cord.

Communitywide access to clean water, sanitation and snail eradication programs can prevent schistosomiasis outbreaks. Praziquantel, a miracle drug discovered in the 1970s, kills both the worms and their eggs in a single dose with minimal side effects. It does not prevent reinfection, but it does prevent serious complications of heavy infection. Unfortunately, all these measures to prevent and treat schistosomiasis are costly, often beyond the means of developing communities. (Happily, the cost of praziquantel recently dropped considerably, increasing access worldwide.)

Schistosomiasis is a disease of poor sanitation, contaminated water, ineffective health systems and unaffordable medications. It threatens impoverished communities struggling to build better lives.

—Kohar Jones

In Mbagam, a rice-farming village on the Senegal River, workers wear awkward rubber boots and take yearly doses of praziquantel to ward off infection with schistosomiasis.



But development had already brought disease. In 1986, the completion of the Diama Dam blocked the saltwater tongue of the Atlantic. Freshwater snails migrated from a nearby lake through a sugar company canal and into the fresh water of the Senegal River, where their population exploded. The human population of the sugar boomtown was also exploding. From 10,000 when the CSS was founded in 1972, Richard Toll's population had more than quintupled by 1988, to an official 50,000 (but closer to 75,000) residents, largely due to immigration. Urban amenities had not kept up. An infected migrant worker is believed to have brought the parasite to Richard Toll. The CSS canals became ground zero in a massive schistosomiasis outbreak.

Although there had been 50 isolated cases of intestinal schistosomiasis among migrant workers between 1970 and 1980, before the dam was built, in January 1988 Diokel Dieng, a government health worker in Richard Toll, diagnosed a new case of intestinal schistosomiasis along the Senegal River. By the end of the year, he had found 29 cases. By the end of 1989, there were nearly 2,000. By August 1990, a full 60 percent of the population of Richard Toll was infected with intestinal schistosomiasis. And it spread. By 1998, schistosomiasis had infected hundreds of thousands of people in the Senegal River region. In many towns and villages, as in Richard Toll, the prevalence rates were just shy of 100 percent—only the youngest children, who had not yet had extensive contact with infected water, remained free of disease. It was the largest public health problem facing the region, greater than the looming threat of AIDS and the constant presence of malaria—and all because of the ecological changes wrought by dams and irrigation.

Still, when I asked Aboubakry Gassama, M.D., the head of the CSS health services, whether schistosomiasis would limit socioeconomic development, he said no. Although most workers were sick with schistosomiasis, there were enough healthy migrant workers desperate for a paycheck to replace them. The limiting factor, he said, was the lack of financial resources to irrigate the land around the river. (Of the 600,000 acres that planners had hoped to irrigate by 2000, only 75,000 were in use—the same number that had been irrigated 10 years earlier). This was not to say that schistosomiasis wasn't a problem. Of every 100 workers waiting on benches that lined the clinic's long concrete hallway, nursing machete wounds from the fields or parasitic lesions from the Senegal River, Gassama

estimated that all but two had schistosomiasis. “If people don't do anything, then in 10 years they are indisposed, and in 30 years they are dead,” he said.

Return to the States

From Mbagam, I took a donkey cart to the main road to catch a *car rapide* to the regional capital of Saint-Louis to take a *sept place* (a seven-seated old Peugeot) back to Dakar to catch my plane home—a century's worth of development compressed into 24 hours. Descending through the cloud cover over New York City, I appreciated the rains that watered the gardens that provided food for farmers and industrial workers alike. I returned to New Haven, where libraries serve as cathedrals of knowledge and the sum of human experience could be consulted to shape future planning. MEDLINE provided information about schistosomiasis and disease outbreak in Senegal. Patton, a professor of epidemiology (microbiology) and one of the original Yale researchers, provided the team's reports.

The schistosomiasis epidemic, I learned, could have been prevented. In 1972, when the OMVS decided to develop the Senegal River, the link between dams and disease was well-established. Nevertheless, dam planning progressed with minimal attention to public health concerns.

In 1978, the Yale researchers warned development planners that schistosomiasis was a “serious public health problem” that, without adequate control measures, “might be aggravated by irrigated agriculture. ... inhibiting both agricultural and economic development.” They recommended a disease surveillance team to track outbreaks and implement immediate control measures. They “strongly urged” that Senegalese groups with “considerable experience” as well as “the necessary trained personnel and mobile units to carry out such work” conduct the health surveys. The only reason the Senegalese weren't already doing this work was that they were “rather short of funds and supplies.”

Unfortunately, as budgets contracted under the SAPs, the recommendations were ignored. Nothing was done to avert the preventable outbreak of schistosomiasis. And a generation later, I arrived in Senegal to ask if schistosomiasis would limit the socioeconomic development of the river region. After my first visit in 1998, I made three more trips to Senegal, with support from the Fund for Investigative Journalism and the medical school's Office of Student

A drought in the 1960s and 1970s drove cattle herders off the dry plains of the Sahel and into the cities. In response, the Senegalese government and its neighbors

resolved to spur agriculture and economic development by building dams along the Senegal River. Development, however, remains elusive.

Research, to explore this question. There was no easy answer, I found. It depended on how you defined development.

For individuals struggling to become masters of their own destiny, schistosomiasis severely limited their progress to greater personal and economic freedom. Sick, they could not work. Without work, they could not pay for health care, school expenses for their children or even food.

For industries struggling to make a profit, schistosomiasis had little impact. There were always healthy workers to replace the sick. The limiting factor for economic development was simply the lack of local money to invest in irrigation, factories and industry. Foreign investors shied away from supporting further irrigation at the edge of a desert.

Instead of boosting macroeconomic indicators, the dams ushered in an era of epidemic infectious disease. Poverty trapped villagers in an endless cycle of infection and reinfection. In retrospect, Patton described it as an “extraordinary example of poor planning.”

The Yale team’s recommendations—disease surveillance, strengthened health systems, implementation of available measures to control disease—remain apt today. Health planning must be part of all development planning.

In Mbagam, where four spigots provided water for up to 3,000 people, Manga continued to violate the very rules she had set to protect the health of the villagers. “Only four flasks a day,” said Manga, bemoaning the daily ration—about eight gallons for each household of up to 30 people. “That’s not enough water for sure. You have no choice but to enter the river. It’s the financial means that we’re missing. Above all, the means.” **YM**

Kohar Jones, M.D. '05, is a resident in family practice at Middlesex Hospital in Middletown, Conn. She plans to publish her medical school thesis under the title *Germes of Progress: Schistosomiasis in Senegal and the Ethics, Politics and Economics of International Health Research and Development in the 20th Century*.

SOURCE: CIA WORLD FACTBOOK

Senegal at a glance

Population	10,852,147
Population living below poverty line	54 percent (12 in the U.S.)
Unemployment	48 percent (urban youth, 40 percent)
Literacy	40.2 percent
Area	117,714 square miles (slightly smaller than South Dakota)
Arable land	12.78 percent

HIV/AIDS prevalence	0.8 percent (7.4 in sub-Saharan Africa)
Infant mortality	56.53 deaths per 1,000 live births (6.5 in the U.S.)
Religion	Muslim, 94 percent Christian, 5 percent indigenous beliefs, 1 percent
Industries	fish processing, agriculture, phosphate mining, fertilizer production, petroleum refining, construction materials





Healthy eating is the linchpin of diabetes prevention and control. At a March workshop community health advisors got some lessons in preparing low-fat dishes.



Promoting health, from the ground up

Part of a national effort to create community health partnerships, a Yale center is working with New Haven churches to prevent diabetes and with a suburban school to stop teen smoking. The goal? Healthier communities invested in their own outcomes.

By Jennifer Kaylin
Photographs by Gale Zucker

In 1997, when Veronica Puleo, R.N., became the nurse at Amity High School in the New Haven suburb of Woodbridge, she was prepared to handle the fevers, sore throats, headaches, sprained ankles and other ailments that routinely afflict students, but there was one health problem that confounded her.

Cigarette smoking was so rampant that school officials imposed a \$65 fine on any student caught smoking in the school. The hard-core smokers chose to try their luck in “Marlboro Country,” a secluded area behind the school where students gathered to light up. If caught there, they faced an after-school detention, with Puleo sometimes presiding.

“For three hours we’d sit and talk,” she says. “They’d tell me how they were coughing up blood, or that they felt awful in the morning until they’d had their first cigarette, or that they couldn’t fall asleep at night until they had a cigarette. They were almost pleading with me. They were so addicted, but had no way to stop.”

At weekly Bible Study meetings, the Rev. Audrey Tinsley, pastor of the Pentecostal Assembly Church of Deliverance in New Haven, spends a few minutes discussing diabetes. “It affects people of color disproportionately,” says Tinsley, herself a diabetic.

Puleo knew she had to do something, but with limited resources and no program geared for adolescents, she was at a loss. “I was spinning my wheels,” she says. Then she learned about the Yale-Griffin Prevention Research Center (PRC).

The PRC is a partnership between the Department of Epidemiology and Public Health at Yale and Griffin Hospital in Derby, where it is headquartered. It was established in 1998 with a \$350,000-a-year grant from the Centers for Disease Control and Prevention (CDC). That allotment grew to \$800,000 annually in the second funding cycle, which began last October. Funding from other sources brings the PRC budget to between \$2 million and \$2.5 million each year.

One of 28 such centers nationwide, the Yale-Griffin PRC collaborates with the community to develop innovative approaches to health promotion and disease prevention. Collectively, the national PRC network conducts about 500 research projects a year on such topics as aging, arthritis, asthma, job safety, nutrition, cardiovascular health, tobacco control, obesity, diabetes prevention and control, school health and violence prevention.

“The PRC model, which was developed about 20 years ago, grew out of a productive period in the history of public health,” says Eduardo J. Simoes, M.D., M.Sc., M.P.H., program director of the CDC’s prevention research centers. “We had conquered a lot of diseases through immunizations. We were making progress in the areas of occupational and environmental health, so the logical next step was to invest in prevention research at the community level.” Besides funding the PRCs, the CDC provides oversight and makes periodic site visits.

Michael H. Merson, M.D., the former dean of public health and the Anna M.R. Lauder Professor of Public Health, is the principal investigator of the CDC grant. He calls the PRC program “one of the most important initiatives the CDC has in this country.” Too often, he says, there’s a divide between academic research and real-world application. “These centers are really critical in bringing the two together, in taking the best in public health knowledge and applying it in a field setting.”

Pizza, soda and cigarettes

When Puleo contacted the Yale-Griffin PRC, she was put in touch with the director, David L. Katz, M.D., M.P.H. ’93, associate clinical professor of epidemiology and public health, who, along with Merson, founded the PRC. “He immediately

took charge of the situation and helped me out,” Puleo recalls. Katz introduced her to scientists doing research on adolescent smoking. He joined her at meetings with students and helped her write a news bulletin for parents. Eventually, their work became a research project on the effectiveness of tailored behavioral interventions and the drug Zyban in fighting adolescent nicotine addiction. Although Zyban has helped adults quit smoking, Puleo says it proved ineffective with her study group. Study findings were published in the journal *Behavior Modification* last year.

What did work was the eight-week program she and Katz developed. Each week focused on a different topic—from what cigarette smoking does to the body and identifying why students smoke to preparing them for withdrawal. Students received gum, pencils and water bottles to fulfill the oral fixation that cigarettes satisfy. Puleo and Katz set out to identify what incentives work best with adolescents. “We gave them a choice: money or pizza and soda at our weekly meetings,” Puleo says. The answer provided some insight into why adult treatment models don’t necessarily work with adolescents. “The money meant nothing; they just use it to buy more cigarettes,” Puleo says. “The pizza and soda was front and center. It allowed them to socialize, which is so important for young people, and gave them something to look forward to from week to week.” Katz, a nutrition expert, was somewhat reluctant to go the pizza and soda route. “But I am a practical guy,” he notes. “I try very hard not to make ‘perfect’ the enemy of ‘good.’ I figured we could get to dietary detox once we helped these kids quit smoking.”

There are now about 60 students enrolled in the program. Katz estimates that between a third and a half either quit smoking or cut back significantly. The PRC stayed involved with the Amity smoking cessation program for about four years, until it could run on its own. “This is the kind of thing we’re hoping to achieve on a larger scale,” Katz says. “A big part of what our center does is to take the knowledge we acquire and translate it into a real-world setting until it can become self-sustaining.”

The Yale-Griffin PRC has generated studies and publications in the area of smoking cessation for adults, and invented a novel behavior modification technique Katz terms “impediment profiling,” which identifies barriers to behavior change. “Then we tailor the intervention components to correspond,” Katz says. “We’ve had success with this approach



in smoking cessation and physical activity promotion, and just received notice of our first grant award to develop the technique for dietary change and weight control as well.”

Another PRC study found positive results with congestive heart failure patients who received a treadmill and access to a cardiac rehab nurse to help them use it. “The participants really liked it, which is proof of principle,” Katz says. “Now we’re looking for collaborators to help us study whether this could reduce the number of hospitalizations and mortality.”

A randomized trial just completed by the PRC found that massage therapy was highly effective for patients with osteoarthritis of the knee. Katz says the next step is to crunch the financial numbers. “Given all the press about the dangers of anti-inflammatory medicine, what if massage is as good, or better? This could lead to a significant policy change. But to get there requires showing not only that it works, but that it’s cost-effective.”

Partnering with the community

Beth P. Comerford, M.S., the PRC’s deputy director, says PRCs focus on different health issues, depending on the needs of the community, but their basic approach is always

the same: partnering with the community. “Everybody at the table holds an equal place and is involved in the decisions being made.” This is a time-consuming and, at times, frustrating process, Comerford concedes, but because the goal is real-world application, it can also be rewarding.

“With the traditional clinical trial model, you’re basically saying, ‘You’re the subject, we do things to you.’ Then we leave,” Comerford says. While researchers may develop the perfect scientific protocol, if it requires test subjects to do something that makes them uncomfortable, such as take a medication or have blood drawn, they may refuse to participate. And any scientific results may not be lasting in real-world settings. “What we do,” Comerford says, “is go to the community at the start and ask them, ‘What are *your* priorities? What would work to address them? What would people be willing to do?’ This is key for participation and sustainability.”

In 2002, the Yale-Griffin PRC embarked on a long-term project called PREDICT (Partners Reducing Effects of Diabetes: Initiatives through Collaboration & Teamwork). While researchers want to determine why information about diabetes isn’t reaching the at-risk population, they know that for this project to succeed, there are side issues they may have to tackle first. “Before you can focus on the health



issue, you may need to work with people on issues related to jobs, child care, housing,” Comerford says.

While it may seem digressive for public health researchers to address such social ills as unemployment, Katz says it’s essential. “If you tell a group of people you want to talk to them about diabetes and they say they’re more concerned about finding jobs and you say, ‘Yeah, well that’s not our thing,’ they’re going to show you the door,” he says. He offers an example from his clinical work: A patient couldn’t quit smoking. The resident physician kept focusing on smoking cessation, but Katz found out she was homeless, and the focus shifted to the patient’s more pressing needs. Three months after she’d moved into a new home, she was ready to quit smoking.

The PREDICT project will evaluate the Community Health Advisor model for getting people at risk to adopt healthier lifestyles. This method identifies natural leaders in a community and trains them to serve as surrogates for health care professionals. “Rather than the traditional we’re-here-to-help-you model,” Katz says, “members of the community spread the gospel.” New Haven will be the test community and Bridgeport will be the delayed control—meaning it won’t get any intervention until after the study is over. A related pilot study seeks to improve the patient-doctor relationship by coaching patients who have been newly diagnosed with diabetes on how to talk to their doctors.

For PREDICT, researchers initially planned to work through the public schools to disseminate information about diabetes, but an advisory committee of community members felt it should be a church-based initiative. “We helped them tweak their structure,” says committee member Sharon Bradford. “We decided they should work through the religious community. We felt there was a captive audience in the churches.” The committee also put researchers in touch with local ministers and helped select and hire a local outreach coordinator to serve as a liaison between the community and the PRC.

That outreach worker is Maurice Williams, who also saw that working through the schools wouldn’t be effective. “When parents go to a school they’re thinking about how their child is doing in school, not about health issues,” he says. “Plus, if you work through the churches the message is flowing from the parent down. The child isn’t carrying all the weight of bringing the information home.”

Twelve African-American churches in New Haven were chosen for the study. Two volunteers from each were recruited as community health advisors. During 10 weeks of training they learned about the causes, symptoms and treatment options for diabetes. They also learned about nutrition, how to read food labels, low-fat cooking techniques and different methods they might use to educate their congregations. Church members were then given a baseline survey to see how much they know about diabetes. The next step, which is under way, is for the community health advisors to go back to their churches and educate their congregations about diabetes. Church members will then be surveyed again to see whether their understanding about diabetes has increased.

“Why don’t they serve fruits and vegetables?”

The Rev. Audrey Tinsley, the pastor of the Pentecostal Assembly Church of Deliverance, signed up as a community health advisor because she has diabetes. “I wanted to learn ways I could keep my diabetes from escalating into something worse, and I wanted to help keep other people from getting the disease,” she says. She spends 15 minutes of every Bible Study period sharing information about diabetes and passes out diabetes literature at her church.

Tinsley now talks about diabetes with a convert’s zeal. “It affects people of color disproportionately,” she says. “It affects us more because of the food we eat. Fast food, junk food, something quick. Diet is the number one thing that causes diabetes.”

When the conversation turns to school lunches, Tinsley’s voice takes on an angry edge. “Pizza, chicken nuggets,” she says. “There’s nothing nutritional here! Why don’t they serve fruits and vegetables? Why don’t the kids have decent food?”

Tinsley isn’t alone. At a meeting of community health advisors in the basement of Bethel AME Church, everyone had stories to tell. Several people talked about their own experiences with diabetes. Food was a recurring subject of conversation—low-fat ways to prepare favorite dishes, the benefits of Mrs. Dash salt substitutes, the merits of cooking collard greens with smoked turkey instead of pork. At one point, someone suggested putting together a cookbook of healthy recipes. One health advisor wrote a skit about diabetes she hoped the group could present at a community

OPPOSITE At the March workshop Sharon Bradford, a member of a community advisory committee, led the group in line dancing. “People think that dancing is just fun, but it’s also movement and exercise,” Bradford says.

BELOW Eggs, says researcher Zubaida Faridi, are a good source of nutrition. At Griffin Hospital in Derby, she uses an ultrasound to measure the effects of egg consumption on the ability of blood vessels to dilate, an indicator of cardiac and vascular health.

event. It contained three scenes; by the end of the meeting it had grown to seven.

When the Yale-Griffin PRC began, it served the six towns of the Lower Naugatuck Valley—Derby, Ansonia, Seymour, Shelton, Oxford and Beacon Falls. One of its early major initiatives was the Valley Health Profile—a collection of data about diseases and causes of death over a three-year period. “The local data helped us see local patterns we used to develop our priorities,” Katz says, noting, for example, that physical activity and fitness levels of Valley schoolchildren were of concern. This information was disseminated among health care agencies to be used for setting priorities. The PRC now produces a “Community Health Profile” every two years, covering not only the Lower Naugatuck Valley,

but also New Haven, Bridgeport and Hartford. In addition, a health newsletter goes out to approximately 40,000 households twice a year.

As the Yale-Griffin PRC has grown, emphasis has shifted away from the Valley, but residents who live near Griffin Hospital still participate in clinical trials. The PRC has about 15 to 20 active projects involving between 200 and 500 participants, mostly from the Valley communities.

One project is looking into the effects of egg consumption on the ability of blood vessels to dilate, a reliable indicator of cardiac and vascular health. The first egg study looked at 50 healthy people from the Valley who ate two eggs a day. “We found that the blood vessel response was normal in both the intervention and the control groups,”



Like other once-thriving industrial towns in the Naugatuck Valley, Derby has fallen on hard times. Health issues in the Valley were the initial focus of the Derby-based Yale-Griffin Prevention Research Center, led by David Katz, which promotes self-sustaining projects for better health.



says clinical research associate Zubaida Faridi, M.D., M.P.H. This means egg consumption did not have a negative effect on the endothelium—the inner lining of the blood vessel—nor did it raise serum cholesterol levels. Faridi is now replicating the study on test subjects with elevated cholesterol levels. “We see this study as having practical applications for a large element of the population,” Faridi says. “Eggs are a very commonly used food, with an excellent nutrition profile, and their exclusion from the diet comes at a cost.”

Katz believes the move toward community-based research models represents a sea change in public health research. “It’s health with and for communities, rather than the paternalistic, ‘Trust us, we’re from an academic environment,’” he says. “Gertrude Stein had it right: ‘A difference, to be a difference, must make a difference.’ For research to make a difference, it must be put to use in the real world.” While Katz says research universities are slow to deviate from their time-tested ways, he sees the PRC’s methodology as the wave of the future, from the standpoint of both public acceptance and financial support.

“I’m hoping we’re tossing a pebble in the pond and that the ripples go to the far shore.” **YM**

Jennifer Kaylin is a writer in New Haven.

Gale Zucker is a photographer in Branford, Conn.

From medicine to media, a doctor extends his reach

After becoming an expert in nutrition, obesity and chronic-disease prevention, David L. Katz, M.D., M.P.H. '93, wasn't satisfied treating patients in his office; he wanted to get the message out to the widest possible audience. That led to his now-flourishing second career as a media star.

It began in 1997 with a health column in the *New Haven Register*, followed by appearances on local TV, and then a monthly health column in *O, The Oprah Magazine*. He contributed articles to magazines and newspapers and was soon appearing on *Good Morning America*, the *Today* show, *48 Hours* and *20/20*. Most recently, he was named medical correspondent for the ABC network, and he will soon begin a nutrition/health column for *The New York Times*.

“I was drawn to the media for the same reason I was drawn to public health: to have the greatest impact on the health of the population,” he says.

A self-described multitasker—Katz, 42, typically works at least 10 hours a day, seven days a week, and once juggled three book deadlines simultaneously—he recognizes that his expanding media obligations will require him to cut back on his clinical and academic duties. He plans to teach a bit less and relinquish his post as director of medical studies in public health at the School of Medicine, which he has held for eight years. He will continue to see patients and to direct Yale's Prevention Research Center.

“What’s mattered to me from the start,” he says, “is making a difference. I’m interested in real-world impact, as soon as possible.” That’s why he sees his work in the media as worthwhile. “We could all but eradicate heart disease,

and greatly reduce the toll of cancer, just by implementing what we already know,” he says. “So the question is: how do we get people to make changes in their lives? One thing that’s clear, you need to reach them. Through my work in the media, I can reach many more people in one day than I could hope to reach treating patients in my office over the span of my entire career.”

Besides teaching, treating patients, writing and making public appearances, Katz is also a successful inventor and poet. Among his inventions—he holds five patents—are an anatomically appropriate bicycle seat, a multi-use winter sport boot for children and a child-safe nail clipper. As an antidote to all his medical writing he turns to poetry, which has been published in anthologies and journals ranging from the strictly literary to *JAMA: The Journal of the American Medical Association*.

Katz, who has five children, says that when he’s not working he enjoys cooking, horseback riding, hiking, skiing and carpentry. His wife, Catherine, a neuroscientist, is collaborating with him on a book about nutrition.

He attributes his productivity to passion for the things he does. “Loving what you do makes all the difference,” he notes.

—Jennifer Kaylin



An assumption with deadly consequences

Throughout the world, health workers find it hard to believe that the disabled are at risk for HIV/AIDS.

Because of the strange sores that had begun to appear on the inside of James' mouth and on his arms, the 28-year-old finally decided to get tested for HIV. Heterosexual, with more than one girlfriend, and living in a region of southern Africa where almost 40 percent of the population is HIV-positive, James had good reason to worry. He begged a neighbor for a ride into town to avoid walking seven hours to the HIV clinic, and once there he waited three hours for his name to be called. As soon as he stepped to the front desk, however, he was dismissed; the nurse had been watching James while he waited, and right away she told him, "You don't need a test; you couldn't possibly have HIV."

When I spoke with James six months later, the wasting caused by the AIDS virus had already begun to take its toll. Like millions of other Africans, this young man would soon die of AIDS. James was different from them in only one way: James was deaf.

The vulnerability to HIV/AIDS of the world's 600 million disabled people has been virtually ignored. Conventional wisdom dictates that people with disabilities are unlikely to be at risk—unlikely to have sex, use drugs or be vulnerable to rape. Yet disabled individuals are at equal or increased risk for all known AIDS risk factors. High rates of poverty and illiteracy and the stigma associated with disability only

increase these risks for the millions of people who live with a physical disability or psychiatric illness or who are blind, deaf or mentally retarded.

As a researcher on disability issues, I suspected that the impact of AIDS on those with pre-existing disabilities was being overlooked. I was unprepared, however, for how little attention this issue had received. A search of the global literature yielded only 38 short articles on the topic.

I wanted to fill this gap. In 2003, with funding from the World Bank I undertook a global survey on HIV/AIDS and disability. We sent it to 5,500 AIDS researchers, rehabilitation programs and disability advocacy groups worldwide. Responses came from 57 countries.

Worldwide, the data showed, AIDS education and outreach programs are extremely unlikely to reach disabled individuals. AIDS radio campaigns do not educate the deaf. Billboard and newspaper campaigns do not reach the blind. With global literacy rates for disabled adults averaging as low as 3 percent (and around 1 percent for disabled women), many disabled individuals can't understand complicated AIDS education messages. For those who do seek testing or medical care, accessibility remains a problem: stairs impede entrance to clinics for those with physical mobility problems.

Concerns do not end there. The assumption that people with disabilities are virgins endangers lives in two ways. In dozens of countries, individuals with disabilities are turned away from testing centers by health workers who assume that they are neither sexually active nor HIV-positive. In many countries they are targeted for rape by

HIV-positive people who believe in "virgin cleansing." Even those diagnosed with HIV are at the bottom of lists for medical care and social support; their lives are considered less valuable than those of people without disabilities.

These results carry a message for clinicians worldwide: they must be aware of the risks that their disabled patients face. Yet people with disabilities find that doctors rarely ask them whether they are sexually active or discuss safer sex, even though their risk of physical abuse and rape is significantly higher than for nondisabled people, particularly in group homes or institutions.

The survey results have fostered increased awareness of HIV/AIDS and disability, and over the past year, a consortium of UN agencies has joined the World Bank and disability advocacy organizations to press for inclusion of a disability component in AIDS outreach and education. My colleagues and I have begun a new series of studies to better identify and evaluate programs for disabled individuals at risk. I hope it will make a difference: the need is immediate, and millions of lives are at stake.

For more information, visit www.cira.med.yale.edu/globalsurvey.

The American Sign Language symbols above spell AIDS.

Nora E. Groce, PH.D., is an associate professor of public health and anthropology in the Global Health Division of the School of Public Health.

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



David Leffell

As deputy dean, Leffell moves practice into 21st century

With his appointment as deputy dean for clinical affairs in February, **DAVID J. LEFFELL, M.D., HS '86**, continues a task he began almost 10 years ago, when he added a new portfolio to his work in the clinic and laboratory. As associate dean for clinical affairs and director of what was then called the Yale Faculty Practice, Leffell sought to improve the business side of medicine. The faculty practice is now the Yale Medical Group (YMG), where recent surveys show improved patient satisfaction, as well as areas where improvement is needed. Most importantly, the YMG has begun to introduce changes in the practice of medicine, helping it move outside traditional departmental boundaries into interdisciplinary, disease-based teams that include researchers as well as physicians.

"Because our knowledge of disease is so much more refined, we understand that solutions to illness are not limited to a particular organ in which the disease is expressed," said Leffell, who will oversee the growth and development of the clinical practice. Among his goals are strengthening ties between clinical care and medical research and spreading the word about Yale's faculty expertise. He also hopes to improve the clinical infrastructure by making it easier for patients to make appointments and by ensuring close communications between referring physicians and specialists.

"To teach medical students to be doctors of the 21st century, to take care of patients with new technology and medications of the 21st century, you have to have a clinical practice of the 21st century," Leffell said.



Kim Bottomly

Bottomly named deputy provost for science, technology

H. KIM BOTTOMLY, PH.D., has been named deputy provost for science, technology and faculty development, effective July 1. Bottomly, who has been at Yale since 1980, is professor of immunobiology, dermatology and molecular, cellular and developmental biology. She also served as acting chair of the Section of Immunobiology. Provost Andrew D. Hamilton, PH.D., announced the appointment in April.

As deputy provost, Bottomly will help shape and implement policies in the natural sciences, anthropology, psychology, statistics and linguistics. She will oversee Yale Engineering, the School of Forestry & Environmental Studies, the Peabody Museum of Natural History, the Yale Institute for Biospheric Studies and the Yale-affiliated Haskins Laboratories. Bottomly will also work on initiatives to increase faculty diversity, improve recruitment and retention of women and underrepresented minorities in science, and enhance career development for faculty.



Thomas Gill



Steven Hebert



Stefan Somlo



Hal Blumenfeld

Three Yale scientists have received close to \$1 million each from the Ellison Medical Foundation to pursue research into infectious disease. The three are among the 10 Senior Scholars in Global Infectious Disease announced in December.

Jorge E. Galán, PH.D., D.V.M., the Lucille P. Markey Professor of Microbiology and chair of the Section of Microbial Pathogenesis, will study the bacterium *Campylobacter jejuni*, one of the most common causes of gastrointestinal infection worldwide.

John R. Carlson, PH.D., the Eugene Higgins Professor of Molecular, Cellular and Developmental Biology, will explore new approaches to the design of repellents and traps for disease-carrying insects.

Ruslan Medzhitov, PH.D., professor of immunobiology and a Howard Hughes Medical Institute investigator, will examine how immune system responses to one infectious agent affect the body's defenses against concurrent infections.

Thomas M. Gill, M.D., FW '94, associate professor of medicine (geriatrics), and **Michael Cappello, M.D., FW '95**, associate professor of pediatrics and epidemiology, have been elected to the American Society for Clinical Investigation (ASCI), one of the nation's oldest and most respected medical honor societies. The ASCI membership includes physician-scientists elected for their achievements in biomedical research.

Two Yale physician-scientists were honored with major awards in the field of kidney research at the World Congress

of Nephrology meeting in Singapore in June.

Steven C. Hebert, M.D., the chair and C.N.H. Long Professor of Cellular and Molecular Physiology and professor of medicine, and **Stefan Somlo, M.D., FW '91**, the C.N.H. Long Professor of Medicine and chief of the Section of Nephrology, are being recognized for important discoveries.

Hebert will receive the A.N. Richards Award, which carries a \$10,000 cash prize, from the International Society of Nephrology (ISN) for three discoveries in the field of ion transport and ion sensing. Somlo will share the Lillian Jean Kaplan International Prize for Advancement in the Understanding of Polycystic Kidney Disease for his work in discovering genes that cause polycystic kidney and liver diseases. Somlo and co-recipient Gregory G. Germino, M.D., HS '87, of the Johns Hopkins School of Medicine will receive \$50,000 each from The PKD Foundation and the ISN.

A third Yale nephrologist, **Walter F. Boron, M.D., PH.D.**, professor of cellular and molecular physiology, has been selected to receive the Homer W. Smith Award, the American Society of Nephrology's top honor for basic research. The award, which carries a \$10,000 cash prize, will be presented at the society's annual meeting in November in Philadelphia.

Two Yale psychiatrists received the American Psychiatric Association's APIRE/Kempff Fund Award for Research Development in Psychobiological Psychiatry at the association's annual meeting in Atlanta in May.

John H. Krystal, M.D. '84, the Robert L. McNeil Jr. Professor of Clinical Pharmacology and



Ronald Breaker



Linda Degutis



Vincent DeVita Jr.



John MacMicking



Bruce McClennan



Anna Marie Pyle



Robert Udelsman



Stephen Waxman

deputy chair for research in the Department of Psychiatry, and **Daniel H. Mathalon**, M.D., PH.D., assistant professor of psychiatry, were recognized for providing new insights into the neurobiology and treatment of cognitive impairments associated with schizophrenia.

In March **Sidney J. Blatt**, PH.D., professor of psychiatry and psychology and chief of psychology in the Department of Psychiatry, in collaboration with colleagues in Belgium, published a book, *The Theory and Treatment of Depression: Towards a Dynamic Interactionism Model*, that grew out of a collaboration begun in 2003. Blatt spent a month that year at the Catholic University of Leuven as a visiting professor. A colleague at Yale, **Paul L. Erera**, M.D., HS '57, professor emeritus of psychiatry and a native of Belgium, sent greetings via videotape.

Hal Blumenfeld, M.D., PH.D., FW '98, assistant professor of neurology, neurobiology and neurosurgery, has received the Dreifuss-Penry Epilepsy Award from the American Academy of Neurology. The award recognizes physicians in the early stages of their careers who have contributed to epilepsy research.

Ronald R. Breaker, PH.D., associate professor of molecular, cellular and developmental biology, has been named a Howard Hughes Medical Institute investigator and the Henry Ford II Professor of Molecular, Cellular and Developmental Biology. Breaker's lab explores the "RNA world," the idea that the Earth's first life forms were composed of RNA rather than DNA. His

studies have led him to discover dozens of regulatory structures, known as riboswitches, which might be used to control the activity of genes inserted into cells during the course of gene therapy.

David C. Cone, M.D., associate professor of surgery (emergency medicine) and public health, was installed as president-elect of the National Association of EMS Physicians at the group's annual meeting in January.

Linda C. Degutis, M.S.N. '82, DR.PH. '94, associate professor of surgery (emergency medicine) and epidemiology and public health, was elected chair of the executive board of the American Public Health Association, the primary association for public health professionals.

Vincent T. DeVita Jr., M.D., HS '66, the Amy and Joseph Perella Professor of Medicine, has been named editor in chief of a new journal for oncologists, *Nature Clinical Practice Oncology*. DeVita previously served as head of the Yale Cancer Center and director of the National Cancer Institute.

Marie L. Landry, M.D., HS '77, FW '81, professor of laboratory medicine and director of the Clinical Virology Laboratory at Yale-New Haven Hospital, received the 2005 Diagnostic Virology Award from the Pan American Society for Clinical Virology in May for outstanding contributions to the field.

Robert J. Levine, M.D., HS '63, professor of medicine and co-chair of the Yale Bioethics Project, has received the Health Improvement Institute's Lifetime Achievement

Award for Excellence in Human Research Protection. Levine has contributed to the literature of the field of protection of human research subjects by publishing over 200 articles and one major monograph and by founding and editing *IRB: A Review of Human Subjects Research*.

John D. MacMicking, PH.D., assistant professor in the Section of Microbial Pathogenesis, has been selected as a 2005 Searle Scholar as part of a program that supports the independent research of young faculty in the biomedical sciences and chemistry. In 2004 MacMicking also received the Mallinckrodt Foundation Program Scholar Award, given annually to young scientists starting their careers. He studies host innate immunity, with an emphasis on the role played by interferon pathways against intracellular infections like tuberculosis.

Bruce L. McClennan, M.D., professor and chair of diagnostic radiology, was elected president of the American Roentgen Ray Society, effective May 15. The oldest radiology society in the United States, it has advanced radiology through annual scientific and educational meetings and the *American Journal of Roentgenology*.

Stephanie S. O'Malley, PH.D., professor of psychiatry and director of the department's Division of Substance Abuse Research, has received the 2004 Dan Anderson Research Award. The award, sponsored by the Butler Center for Research at the Hazelden Foundation, honors researchers who have advanced the study of addiction recovery.

Anna Marie Pyle, PH.D., has been appointed the William Edward Gilbert Professor of Molecular Biophysics and Biochemistry. Her research explores how RNA folds and organizes itself to catalyze reactions. Since 2002, Pyle has also been a Howard Hughes Medical Institute investigator.

The Bayer Pharmaceuticals Corp. has given the 2004 Bayer Award to **Raymond R. Russell**, M.D., PH.D., FW '00, assistant professor of medicine (cardiology). Russell studies cardiac function and metabolism and the changes associated with disease states.

Robert Udelsman, M.D., M.B.A., the Lampman Professor of Surgery and Oncology and chair of surgery, was elected president of the American Association of Endocrine Surgeons. Membership includes surgeons who devote significant portions of their practice or research to endocrine surgery and who are certified by the American Board of Surgery.

Stephen G. Waxman, PH.D., M.D., professor and chair of neurology and professor of pharmacology and neurobiology, has been named the Bridget Marie Flaherty Professor of Molecular Neurology. Waxman, a renowned neurologist and molecular neuroscientist, studies the roles of sodium channels in multiple sclerosis, spinal cord injury and neuropathic pain.

SEND FACULTY NEWS TO
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to claire.bessinger@yale.edu

The Class of '05



TERRY DAGRADI (3)

ABOVE Medical students sported toy stethoscopes as a symbol of their calling.

OPPOSITE LEFT Graduates Mariah Ruth and Michael Shapiro joked with Associate Dean Nancy Angoff before the procession to the main campus.

OPPOSITE RIGHT Helena Hansen, who graduated from the M.D./PH.D. program, took her daughter, Kirin, onstage as she received her diploma.

An unfinished agenda: keeping people healthy

At Commencement, a former surgeon general urges access to health care and sex education.

Growing up in a small town in Arkansas, M. Joycelyn Elders, M.D., never saw a physician until she went to college. But in 1993 she became the nation's top doctor, and as surgeon general her outspoken support of sex education provoked controversy. Access to knowledge about sexual health issues was a theme she echoed in her Commencement address at the School of Medicine in May, and the crowd loved it.

Elders told the 96 graduating students—who offered standing ovations at the beginning and end of her address—that an increase in HIV infections, rising rates of sexually transmitted diseases and the highest teenage pregnancy rates in the industrialized world prove that there's an important place for sexual-health education in schools. "You can't

keep people healthy if you don't educate them," said Elders, professor emeritus of pediatric endocrinology at the University of Arkansas for Medical Sciences. "And you can't educate them if they're not healthy."

Although she has long advocated abstinence, she also feels that young people need to know about safe sex. "The vows of abstinence," she told the cheering crowd, "break far more easily than a latex condom."

She also cautioned the graduates that, despite having the best medical education, the best training, the best hospitals and the best colleagues in the world, they have a huge unfinished agenda. "We need to make sure we have improved access to care for all of our people," she said, noting that more than 40 million people in the United States lack health insurance. Elders ended on a note of optimism, asking the graduates to use their power, prestige and position in their communities to effect change.

At the Commencement on Harkness Lawn, the Class of 2005



The Class of 2005 chose Joycelyn Elders, who served as surgeon general under President Clinton, as its keynote speaker.



JOHN CURTIS





TERRY DAGRADI



JOHN CURTIS

TOP Stephanie Colegio-Eisenbarth celebrated with her husband, Oscar Colegio, who graduated from the medical school last year.

ABOVE Inna Landres and Michele Flagge before the university ceremony on Old Campus.

honored Robert D. Auerbach, M.D., HS '87, lecturer in obstetrics, gynecology and reproductive sciences, with the Francis Gilman Blake Award for outstanding teaching. Jennifer M. Gaudiani, M.D., a resident in internal medicine, received the Betsy Winters House Staff Award, given to the resident who has made the most significant contribution to the education of medical students. This year's class gift was the largest ever: \$2,000 was given to the Society for Distinguished Teachers, and \$2,000 was pledged to the medical school's endowment for scholarships, an amount that will be matched by the university.

The Bohmfalk Prize for teaching basic sciences was awarded to a husband-and-wife team for the first time: Marie L. Landry, M.D., HS '77, FW '81, professor of laboratory medicine, and Peter S. Aronson, M.D., FW '75, the C.N.H. Long Professor of Medicine and professor of cellular and molecular physiology. The Bohmfalk Prize for teaching clinical science went to Michael K. O'Brien, M.D., PH.D., assistant clinical professor of surgery (gastroenterology). Sharon K. Inouye, M.D., M.P.H. '89, professor of medicine, received the Leonard Tow Humanism in Medicine Award, while Catherine Chiles, M.D., associate clinical professor of psychiatry, won the Leah M. Lowenstein Prize, which recognizes faculty who promote humane and egalitarian medical education. The first annual Alvin R. Feinstein Award for outstanding clinical skills was awarded to Ronald R. Salem, M.D., associate professor and chief of surgery (oncology).

—Jill Max

An “old-fashioned” idea: nothing is more important than the public health

Fast Food Nation author Eric Schlosser peered at the 107 public health students gathered for Commencement in Battell Chapel on May 23 and called them “strange.” In a culture that insists that “everything is better when it’s for profit,” he said, these new graduates of the School of Public Health believe in “incredibly old-fashioned” ideas: the public good, the public interest and public service.

“There is nothing more important than the public health,” said Schlosser, a journalist whose bestselling book describes how the fast food industry has transformed America’s diet and its economy. “We have lost sight of this basic truth, and the greed and the selfishness of the past two decades have obscured it.” Even the wealthiest will not be safe from what Schlosser calls “the great levelers of mankind: the viruses and microbes that don’t really care where you went to school.”

Good public health saves money in the long run, said Schlosser. Just as disease mapping helped pioneering epidemiologist John Snow, M.D., discover the water pump responsible for much of a London cholera outbreak in 1854, modern maps would locate the American public health crisis in the poorest neighborhoods. “It is an illusion—a dangerous illusion—to think that the poor health of the poor can be ignored. We will all pay for it one way or another,” said Schlosser, noting that microbes from a sick busboy can find their way into the finest of gourmet meals.



JOHN CURTIS (5)



In closing, Schlosser told the graduates, “We need more strange people like you. I have enormous respect for the path you have chosen.”

Also speaking was graduate Reshma Trasi, who told her classmates to persist despite barriers and to listen. “The next time you want to say something, try stopping yourself and letting the other person talk. ... It will open your mind.”

The students chose Elizabeth H. Bradley, M.B.A., PH.D. '96, associate professor of public health, for the Award for Excellence in Teaching, her third in her nine-year career at Yale.

Other awardees included Lisa M. DiFedele, Farnoosh Hashemian, Asa Margolis and Bonnie E. Gould Rothberg, M.D. '94, HS '96, each of whom received a Dean's Prize for outstanding master's thesis.

The Wilbur G. Downs International Health Prize went to Anna Beitin; the Henry J. (Sam) Chauncey Jr. Inspiration Award to Elinor Schwimmer; and the Cortlandt Van Rensselaer Creed Award to Edward Magee and Anika Hines.

—Cathy Shufro

CLOCKWISE FROM TOP LEFT

Before the ceremony on Old Campus, public health student Koren Odierna helped Aruna Dhara adjust her stole as Nabila Alibhai watched.

Fast Food Nation author Eric Schlosser, left, with public health Dean Brian Leaderer, said in his Commencement address that the health of the poor cannot be ignored. Viruses and microbes, he said, are “the great levelers of mankind.”

Elizabeth Bradley received the award for excellence in teaching.

Kevin Neill waited with classmates for the procession into Battell Chapel.

Reshma Trasi, who gave the student address, was joined by her family at the ceremony at Battell Chapel.



Match Day sees more bound for New Haven residencies and training as generalists

While many people celebrated March 17 as St. Patrick's Day, medical students from the Class of 2005 had another reason to celebrate. There were shouts, cheers and tears of joy at Harkness Ballroom on Match Day, the half-century-old ritual that will likely determine the course of their careers. Nationwide, almost 94 percent of medical school seniors matched to residencies this year.

Students applied to programs around the country, but a larger number than ever before—27 out of 94—are staying in Connecticut, mostly at Yale-New Haven Hospital. "People worry about New Haven—is it keeping good students? Well, it's keeping really good students," said Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93, associate dean for student affairs. Another trend at Yale is that more students this year are going into internal medicine, primary care and pediatrics than in past years, which saw higher numbers of graduating seniors entering surgical subspecialties.

For the most part, students were calm and poised as they approached the

tables stacked with the envelopes that held news of their futures for the next four years. But Michael Shapiro was unable to contain himself as he sprinted ahead of the crowd, ripped open his envelope, let out a yell and then burst into tears. He was accepted to the University of Pittsburgh Medical Center's plastic surgery program, his goal after volunteering for Operation Smile two years ago, when he went to Morocco to assist with reconstructive surgery. "It sounds schmaltzy," he said, "but it's been my dream."

Many students whipped out cell phones to share the good news with family and friends, but Brad Raphael was able to share it in person with his father, Irving G. Raphael, M.D. '71, who was on hand. "It's excitement, nervousness and relief all combined into one," the younger Raphael said before opening his envelope. Upon learning the good news—that he was going to the Hospital for Special Surgery at Cornell University Weill Medical College to pursue orthopaedic surgery—he hugged his father, also an orthopaedist, and said, "It's exactly where I want to be. I'm feeling euphoria right now."

—Jill Max



Douglas Jacobson, Michele Flagge, Christopher Kwong, David Ornan, Brendon Graeber, Suzanne Baron and Christopher Lee toasted their matches.



Brad Raphael was joined by his father, Irving Raphael, an orthopaedist who graduated from the medical school in 1971.

2005 residency placements for Yale medical students

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

California

Harbor-UCLA Medical Center, Torrance
Leo Kim, medicine-preliminary

Stanford University Programs

Jeffrey Chi, internal medicine
Douglas Jacobson, medicine-preliminary
Inna Landres, obstetrics and gynecology
Christopher Lee, diagnostic radiology
Nir Madiano, internal medicine

UCLA Medical Center, Los Angeles

Eddiong Ikpe, emergency medicine/internal medicine

University of California,

San Francisco
Neelendu Dey, internal medicine
Jessica Yager, internal medicine

University of Southern California, Los Angeles

Leo Kim, ophthalmology

Colorado

HealthONE Presbyterian/St. Luke's Medical Center, Denver
Mariah Ruth, transitional

University of Colorado School of Medicine, Denver

Heidi Cook, obstetrics and gynecology
Mariah Ruth, dermatology

Connecticut

Hospital of Saint Raphael's, New Haven

Annika Dronge, transitional
David Ornan, transitional

Middlesex Hospital Program, Middletown

Kohar Jones, family practice



JAKE WYMAN (5)

LEFT TO RIGHT Edidiong Ikpe and Niya Jones were ecstatic with their matches. Ikpe is pursuing emergency medicine and internal medicine at UCLA and Jones is doing an internal medicine residency at the Hospital of the

University of Pennsylvania. Erin Mahony shared her news—a residency in pediatrics at Mass General. News of his residency brought Michael Shapiro to tears of joy.

Yale-New Haven Hospital

David Aversa, psychiatry
Anamika Chaudhuri, internal medicine
Stephanie Colegio-Eisenbarth, laboratory medicine
Gina Constantine, internal medicine/primary
Vicente Diaz, ophthalmology
Annika Dronge, ophthalmology
Thomas Fernandez, psychiatry-adult/child
John Forrest, internal medicine
Adam Gafni-Kane, obstetrics and gynecology
Barton Kenney, pathology-anatomic and clinical
Brett King, dermatology
Eleanor Knopp, dermatology
Christopher Kwong, internal medicine/primary
Catherine Loerke, surgery-preliminary
Javier Lopez, obstetrics and gynecology
Coerlida Louis, internal medicine/primary
Ernest Mandel, internal medicine
Deanne Nakamoto, medicine-primary-preliminary, ophthalmology
Sarah Nikiforow, internal medicine
Damani Piggott, medicine/pediatrics
David Ross, psychiatry
Isaac Sasson, obstetrics and gynecology
Grace Smith, medicine-preliminary
Curtis Weiss, internal medicine
Carlos Wesley, emergency medicine

Florida

Jackson Memorial Hospital, Miami
Matthew Whitley, otolaryngology

Georgia

Emory University School of Medicine, Atlanta
Michele Flagge, emergency medicine
Andre Matthews, emergency medicine

Hawaii

University of Hawaii Program, Honolulu
Christoph Lee, transitional

Indiana

Indiana University School of Medicine, Indianapolis
Nicholas Countryman, dermatology

Iowa

University of Iowa (Des Moines) Program
Andrew Chen, medicine-preliminary

Maryland

Johns Hopkins Hospital, Baltimore
Yuri Agrawal, surgery-preliminary, otolaryngology
Amy Duffield, pathology
Naudia Lauder, internal medicine
Martine Solages, pediatrics

Massachusetts

Beth Israel Deaconess Medical Center, Boston
Jillian Catalanotti, internal medicine
Dagan Coppock, internal medicine
Eric Golding, internal medicine
Joshua Klein, medicine-preliminary

Boston University Medical Center

Katherine Gergen Barnett, family practice

Brigham and Women's Hospital, Boston

Cristina Baseggio, internal medicine/primary
Michael Herce, internal medicine
Eleanor Knopp, medicine-preliminary
Janelle Luk, obstetrics and gynecology

Harvard Combined Program, Boston

Susan Rushing, pediatric neurology

Massachusetts General Hospital, Boston

Suzanne Baron, internal medicine
Brett King, medicine-preliminary
Mandy Krauthamer, internal medicine/primary
Erin Mahony, pediatrics
Brian Nahed, surgery-preliminary, neurosurgery

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

Joshua Klein, neurology

Massachusetts General Hospital (Harvard Combined)

Ariel Frey, medicine/pediatrics

Michigan

University of Michigan Hospitals, Ann Arbor
Raymond Lynch, general surgery

Mississippi

Keesler Medical Center Program, Keesler AFB
Kwabena Blankson, pediatrics

New Hampshire

Dartmouth-Hitchcock Medical Center, Lebanon
Daniel Gibson, surgery-preliminary, neurosurgery

New York

Albert Einstein College/Montefiore Medical Center, Bronx
Margo Simon, family practice

Flushing Hospital Medical Center

Daniel Khaimov, transitional

Hospital for Special Surgery/Cornell Medical Center

Bradley Raphael, orthopaedic surgery

Mount Sinai Hospital

Jocelyn Soffer, psychiatry

New York-Presbyterian Hospital-Columbia

Rohit Chandwani, general surgery
Daniel Khaimov, anesthesiology
Aimee Lee, internal medicine

New York-Presbyterian Hospital-Cornell

Jennifer Davids, general surgery
Matthew Davids, internal medicine
Elena Gimenez-Hubbard, surgery-preliminary, urology
Edison Machado, internal medicine/primary

New York University School of Medicine

Helena Hansen, psychiatry
David Ornan, diagnostic radiology

NYU Downtown Hospital

Vicente Diaz, medicine-preliminary

Sound Shore Medical Center of Westchester, New Rochelle

Neil Lester, medicine-preliminary

Staten Island University Hospital

Neil Lester, diagnostic radiology

University of Rochester/Strong Memorial Hospital

Lorky Libaridian, medicine/pediatrics

North Carolina

Duke University Medical Center, Durham
Hardean Achneck, general surgery
Richard Chung, medicine/pediatrics
Sean Lee, general surgery

University of North Carolina Hospitals Program, Chapel Hill

Jesse James, internal medicine
Trevor Phillips, emergency medicine

Pennsylvania

Children's Hospital of Philadelphia
Frances Balamuth, pediatrics
Christina Lynch, pediatrics-preliminary, pediatric neurology

Hospital of the University of Pennsylvania, Philadelphia

Niya Jones, internal medicine
June Spector, internal medicine/primary

University of Pittsburgh Medical Center

Michael Shapiro, plastic surgery

Washington

University of Washington Affiliated Hospitals, Seattle

Chloe Atreya, internal medicine
Andrew Chen, ophthalmology
Jing Feng, dermatology
Sharon Gill, internal medicine/primary
Lianne Hirano, internal medicine
Douglas Jacobson, ophthalmology

Wisconsin

Medical College of Wisconsin Program, Milwaukee

Matthew Streckert, emergency medicine

St. Joseph Regional Medical Center, Milwaukee

Jing Feng, transitional

Three students are pursuing career opportunities other than residency. Julie Cantor will be an associate at Munger, Tolles & Olson, a law firm in Los Angeles. Eric Poolman has a public health postdoctoral fellowship at the School of Medicine. Louis Moreno has a position as research manager at Gerson Lehrman Group, a firm in Manhattan that specializes in customized research for business.

Boffo reviews for Golden Probe!! Raves for Alpern!! Überstein rocks Harkness!!

The excitement was palpable at the *First Annual Golden Probe Awards*, the Class of 2007's entry in the ever-popular parade of shows put on annually by second-year medical students at Yale. Fans gathered behind a rope line at the entrance to Harkness Auditorium to greet the nominees and wonder who among them would win the statues of gilded hands with erect index fingers honoring the best in the business. Fans cheered and snapped photos at the sight of celebrity docs on the other side of the rope.

Inside, it was all about entertainment, not to mention the minutiae of being a medical student. The nod for Best Situation Comedy went to *Seinfeld* XXY, a spoof melding the television show *Seinfeld* with Klinefelter XXY syndrome, a common chromosomal abnormality. *Erotic Admissions* took the award for Best Pornographic Film (heavens!), with a cast starring admissions dean Thomas L. Lentz, M.D. '64, and adult-film actress Jenna Jameson, portrayed by Danielle Guez, as an applicant willing to get into med school "at any cost." (Line from script: "The MCAT is so long and hard!") There was even an award for Best Physiology Textbook, pitting Costanzo's *Physiology*, a top-rated text for med students, against *Medical Physiology* by local heroes Boron and Boulpaep. It ended in a tie.

Dean Robert J. Alpern, M.D., made his Yale singing debut with the theme song from *Dean Alpern's Neighborhood*, the winner of Best Children's Show, which evoked the late Fred Rogers,

BELOW Caryn St. Clair, Cicely Williams and Danielle Guez sang and danced the show finale, "Bust Your Ass," based on the 1990s Young M.C. hit: "This here's a jam for all the students, tryin' to get by, but it's such a nuisance, get shut down cuz of your impudence. Studying a bit would show some more prudence."

MIDDLE Ryan Kelly sang "Hey, Yale," a song about the Yale System, to the tune of Outkast's "Hey Ya."

BOTTOM Michael Martinez of Überstein, a band with four medical students and one public health student, brought down the house with one original song and covers of oldies adapted to medical themes.



TERRY DAGRADI (3)



complete with nerdy sweater and blue tennis shoes. The rock band Überstein raised the roof with their original composition, "New Haven Blues," and the musicians—Michael Martinez and Eric Huebner on guitars, Brian Yablon on keyboards, Dario Englot on bass and public health student Jared Novak on drums—played the four nominations for Best Oldies Song. The titles? "This Glans is Made for You and Me," by Woody Urethrie; "Doc Around the Clock," by Bill Frist and the Congress; "Here Comes the Shunt," by the Needles; and "Don't Know Much" by Cram Booke.

When it came to the cluelessness that defines at least a part of second year, the last entry said it all:

Don't know much biochemistry
Don't know much physiology
Don't know much about a histo book
Don't know much about those pills you took ...

Of course that will all change in two years, when the singers and dancers of '07 will have traded their status as resident comedians for the real drama of residency. Stay tuned!

—Cathy Shufro



Balancing the bedside and the bench, and having fun along the way

As he delivered the 18th annual Farr Lecture at Student Research Day in May, Arthur L. Horwich, M.D., HS '78, FW '83, described his own path to a career in research. He trained as a pediatrician, but the lure of the laboratory ultimately proved too strong to resist. Still, he found a balance, he said. "Research and the bedside," he said, "are inextricably linked." Horwich, a geneticist whose work has shown how proteins fold, still consults on clinical cases.

"You cannot predict exactly what you will be doing in some balance of research and clinical medicine," said Horwich, the Eugene Higgins Professor of Genetics and professor of pediatrics, as he offered some advice. "Make sure it is a balance that really causes you to have fun."

Among the 75 students who presented this year was second-year medical student Mary Dombrowski, who examined whether transplants of olfactory ensheathing cells can regenerate myelin. She chose the topic because her father has multiple sclerosis. In her experiments with rats she found that the cells did encourage myelin growth. "It has stimulated my interest in neurology as a career choice," she said.

Fourth-year student Hardean E. Achneck found the bright side to a devastating disease. Ascending aortic aneurysms are associated with a decrease in systemic atherosclerosis, and there may be a genetic mechanism involved, he said. "If we find out what

BELOW The five students chosen to make oral presentations—Eric Poolman, Raymond Lynch, Margo Simon, Suzanne Baron and Joshua Klein—joined John Forrest, director of student research, keynote speaker Arthur Horwich and Dean Robert Alpern before their talks.



TERRY DAGRADI (3)

MIDDLE David Ross studied the phenomenon of perfect pitch.

BOTTOM Jenna Giltne described her research in protein expression to Linda Bi.

the genes are, we may find the mechanism of this and, eventually, treat atherosclerosis," he said.

Research topics ranged from a mix of basic science and clinical findings to at least one offbeat subject. David A. Ross, a student in the M.D./PH.D. program, studied the phenomenon of absolute pitch. "The vast majority of great composers," he said, "have had perfect pitch." Alison H. Norris, also an M.D./PH.D. student, studied the HIV risk for workers on a sugar plantation in Tanzania. Helena Hansen, who completed the M.D./PH.D. program in May, studied faith-based substance abuse treatment in a Pentecostal community in Puerto Rico.

Five students were chosen to make oral presentations: Margo D. Simon, Eric Poolman, Suzanne J. Baron, Raymond Lynch and Joshua Klein.

—John Curtis



When he's not caring for children, pediatrician Richard Dormont is often out birding near his home in Minot, North Dakota.

65 years out of Yale and still practicing

History taking and the physical exam remain at the heart of pediatrician Richard Dormont's practice.

In Minot, N.D. (population 36,567), the local tourism board had to make up a slogan to help outsiders remember the place's name. (*Why not Minot?* rhymes when pronounced correctly.) Yet the small north-central North Dakota town draws families from large cities in surrounding states and Canada who come seeking medical help for children with hard-to-diagnose diseases. They come to consult pediatrician **Richard E. Dormont, M.D.** '40. Still in practice at the age of 89, Dormont enjoys a reputation as a brilliant diagnostician as well as a dedicated doctor available to patients at all hours. For several years, he has had a reduced patient load and shorter office hours, which allows more time for bird-watching and for visiting his four daughters. But retirement is not on his radar.

"I like keeping busy and using my skills," Dormont said, 65 years after earning his medical degree.

A voracious reader of journals and a regular at medical conferences, Dormont is scrupulous about keeping up with new science. But he believes passionately that the tools he relied on in the early days of his practice—history taking and physical examination—remain the bedrock of medicine. Recently a couple raised in Minot brought their 19-month-old child home to consult Dormont after several physicians were puzzled by the child's breathing problems. He made the potentially lifesaving diagnosis of con-



ERIC STERUD

genital heart disease with equipment no more high-tech than a stethoscope and his own ears. The other doctors, Dormont said, had focused on breathing problems and examined the lungs rather than the heart. In addition, he said, physicians nowadays too often fail to perform a thorough physical exam.

Minot parents keep bringing him their newborns for routine care. "Every time someone has a new addition, they say, 'Now you can't retire until so-and-so's 18!,'" said Leann Hayton, L.P.N.

Hayton met Dormont in 1968 when she came to work in pediatrics at Trinity Hospital in Minot. At first, Dormont's "encyclopedic" knowledge was intimidating, but he quickly put her at ease. "Dr. Dormont is a wonderful and patient teacher," she said. "I learned more listening to and working with him than I could have in any amount of schooling."

Ruth Ann Rexine, R.N., also came to know Dormont through hospital

pediatrics. She remembers his routine of making rounds before 7 a.m. (after breakfasting over medical journals), spending the day in his office, then doing rounds again at 5 p.m. If a child's condition worsened, day or night, Dormont would be at the hospital in minutes. "Always in a suit and bow tie," Rexine remembered.

She chose Dormont for her own children because of his legendary thoroughness, his custom of answering parents' questions by phone every morning from 8:30 to 9 a.m. and for the way he could put children at ease.

Dormont had initially planned to pursue a career in internal medicine. But when he lost the residency he wanted, his pediatrics professor came to the rescue with a job in the pediatric outpatient department at Johns Hopkins Hospital. He saw diseases that have disappeared or are a rarity—polio, measles, mumps—and each of the 55 patients he saw every day got a

Last November David Graham told a Senate committee that the Food and Drug Administration had mishandled the drug Vioxx, which he considered dangerous.

physical examination. “It can be done,” Dormont said.

After Johns Hopkins, Dormont taught at Louisiana State University for two years, but decided academic medicine was not for him. “You have to be a politician,” he said. “I’m the world’s worst politician.”

Dormont served in the South Pacific during World War II and also practiced briefly in Texas. In 1953 he came to Minot, drawn by the chance to work in a group clinic. “That was almost considered communist on the East Coast,” he remembered.

But the practice suited him because it provided him with his own lab, was connected to a hospital and, most importantly, allowed him his own medical library.

Dormont has spent the later years of his career in solo practice. “That can be dangerous,” said James Moller, M.D., a University of Minnesota pediatric cardiologist who regularly comes to Minot for consultations. But, said Moller, Dormont is so intellectually rigorous that he challenges himself the way a good partner would. “He is always questioning, looking up things, studying,” Moller said.

Known universally as “Dr. Dormont,” he has cared for most of his community at one time or another.

“Whenever I’m birding, someone will stop and say hello. Usually it’s one of my patients,” Dormont said.

He estimates that he’s seen several hundred thousand patients during his career. As long as they keep seeking him out, he said, his practice will stay open.

—Colleen Shaddox

FDA’s top safety critic keeps a watchful eye on the public good

Whenever **David J. Graham**, M.D., M.P.H., HS ’81, wonders whether he made the right career move from Yale-New Haven Hospital resident to resident critic of the Food and Drug Administration (FDA), he recalls with remorse a patient who died under his care.

At the time, 1979-1981, he was doing a residency in internal medicine at Yale after graduating from the Johns Hopkins School of Medicine and planning to become an expert on viral infections of the central nervous system. But the patient died of an unexpected adverse drug reaction, and even though Graham was not at fault, “I was the person who had prescribed the drug,” Graham says. The incident “contributed to my interest in studying drug safety.”

He also discovered during his time at Yale that he “didn’t enjoy the day-to-day grind of patient care,” so he settled on epidemiology. Since then, he has had a 20-year career as an epidemiologist at the FDA, forgoing more lucrative

offers in the private sector. He is now associate director for science and medicine in the agency’s Office of Drug Safety. Despite (and because of) that title, he has also become the FDA’s most vocal and listened-to critic.

For years, Graham, 51, has been the FDA’s equivalent of an ingrown toenail, causing his employer pain as he went public with allegations that the agency was allowing prescription drugs it approved to stay on the market despite evidence from its own researchers that the medications were harming and killing people by the thousands.

In Graham’s view, the drug safety problems began in 1992 with the passage of a law aimed at getting lifesaving drugs onto the market faster. To speed up approvals, the law forced pharmaceutical companies to foot most of the bill for the review process. That left the FDA “captured by industry,” says Graham. “He who pays the piper calls the tune.” In the meantime, the same officials who approved the drugs were being asked to monitor their safety after they’d hit the market. If there’s evidence of harm, “now



REUTERS/KEVIN LAMARQUE

they've got to do an about-face," he says. "At its heart, that is an inherent structural conflict of interest."

Graham said a former boss told him that the drug industry was the FDA's client, but Graham, an assistant scoutmaster and devout Catholic with six children, didn't buy it. If he sees that a drug may be harmful, he'll investigate. If the evidence warrants it, he'll challenge the FDA's regulatory position internally, even if it earns him the enmity of his superiors, which it often has. The FDA labeled one of his studies "junk science," and forbade him to publish it in a major medical journal. (Six weeks later the FDA changed its mind and the article was published, last February, in *The Lancet*.)

Graham has called for the withdrawal of a dozen prescription drugs, and almost all of them have since been removed from the market—often after a fight with his superiors—in some cases by the drugmakers themselves. One case made Graham a star witness before the United States Senate's finance committee in 2004, when Merck & Co. suddenly removed Vioxx, its popular painkiller, after the company's studies showed a higher risk of heart attacks and strokes among users of the drug. Graham had been warning about Vioxx for years, but the FDA refused to pull the drug on his recommendations. He testified that the agency also urged him to change the conclusions of another damning study about Vioxx just before Merck's surprising announcement. The voluntary withdrawal placed the agency in an unwelcome spotlight over its alleged failures to protect Americans against unsafe drugs. Meanwhile, Graham

sought whistleblower status, and telephone calls disparaging him to the Government Accountability Project, a nonprofit that protects maverick insiders, were traced back to the FDA. (FDA officials say they allow employees to speak their minds, and couldn't explain the incident.)

"The FDA has let the American people down and, sadly, betrayed a public trust," Graham told the Senate committee.

"I think I've had a substantial impact, as much as FDA officialdom wants to bad-mouth me," he says. "I point to the evidence and I say, 'Look, I'm almost always right.' I don't recklessly recommend the withdrawal of drugs."

He says he hopes to finish his career at the agency, even if more difficulty lies ahead. He has two suggestions for improving drug safety. First, the government should create a drug safety center parallel to the FDA's drug approval center. The new center would oversee postmarketing regulation and would be able to call on the FDA commissioner to pull a drug it deems unsafe. Second, this center should be provided with enough money to do its job. (A bipartisan Senate bill co-sponsored by Democrat Christopher J. Dodd of Connecticut and Republican Charles E. Grassley of Iowa would do just that.)

"I feel fairly certain that I've probably saved more lives taking the career path I have taken than I would have with another career path," Graham says. "That's something that colleagues both within government and in academia remind me of periodically when I tell them of my tales of woe at the FDA—they remind me that I'm doing good."

—John Dillon

With an interest in the past, admissions dean doubles as a chronicler of local lore

Two years after receiving his medical degree, **Thomas L. Lentz, M.D. '64**, made the decision, along with his wife, Judith, to leave New Haven and move to the country. They found a pre-Revolutionary War house in Killingworth, Conn., about 40 minutes from Lentz's job as an instructor in anatomy at the School of Medicine. (When the medical school offered him a position he decided not to pursue a residency.)

Soon everything started growing: the Lentz family, the size of their new home, the Ohio native's involvement in his adopted community and his role at the School of Medicine, where he is now associate dean for admissions and financial aid and professor of cell biology.

On moving day the Killingworth house was "livable," but needy. "There was a lot of work to do," said Lentz. "It never ends." He painstakingly restored an antique barn that was reduced to its stone foundation. He and his wife bought surrounding parcels as they became available. Today their place in the country is an 80-acre spread that requires a great deal of landscaping work, though the five sheep they raise for wool keep the grass trimmed.

Restoring a 1759 house piqued Lentz's interest in Killingworth history. He was a founding member of the historical society and serves as historian of the Congregational Church in Killingworth. (He also is a member of the town's land trust and an elected member of the planning and zoning commission.) In 1976 when the his-

torical society was raising funds to restore a 19th-century schoolhouse, Lentz assembled a pamphlet of old photographs from the town that sold for \$5. This year a copy sold on eBay for \$180. Clearly, there is a market for vintage Killingworth images. So in another attempt to enrich the historical society, Lentz wrote *A Photographic History of Killingworth*, a much more ambitious project. The softcover book features more than 200 photographs along with his narrative.

Lentz said that he wrote the book “in his spare time,” a curious choice of words for a man with teaching responsibilities, his own research interests and a passionate commitment to selecting applicants who will be not only exceptional physicians, but also leaders in their profession. “It never gets old and stale, because there’s always something new,” Lentz said of his interactions with students and applicants. “These kids are doing such amazing things that it’s really exciting to talk with them. I wish I could take them all.”

The typical applicant has changed since Lentz began serving on the admissions committee in 1968. Today many arrive at the medical school with postcollege experience working in health care as well as authorship of one or more scientific articles. Lentz wondered whether the medical school would accept him today.

“We went to college, we majored in biology, maybe we belonged to the premed club. We worked summers as an orderly in a hospital. We might have worked a semester in the lab,” Lentz said.

Lentz is particularly suited to admissions as “one of the staunchest sup-

porters of the Yale System,” said James D. Jamieson, M.D., PH.D., professor and past chair of cell biology. “It’s been a joy to work with him, because I’ve learned so much from him.”

Jamieson is impressed with Lentz’s low-key style in the lab and classroom. With some students coming from humanities backgrounds, Lentz’s thorough, methodical teaching of histology leaves each student excellently prepared, said Jamieson. Lentz fine-tunes lectures he has given literally hundreds of times, added Jamieson, to incorporate new information and increase his effectiveness.

While Lentz’s students still spend time bent over traditional microscopes, his lab also uses a “virtual microscope”—high-resolution scans of slides that students can view and manipulate on computer screens. The new technology makes it easier for students to work together and with faculty, as everyone is viewing the same image simultaneously.

The soft-spoken professor is slow to speak about his own accomplishments but quick to talk about his department, which began as a section in 1973 under the leadership of Rockefeller University scientist George E. Palade, M.D., who would win a Nobel Prize two years later. In addition to pursuing his own research on primitive nervous systems, structure-function relationships of the nicotinic acetylcholine receptor and, more recently, the entry and transport of rabies virus in neurons, Lentz serves as the department’s historian—he stores departmental photographs and papers and wrote a history of cell biology at Yale for the department website.

In the almost 40 years that Thomas Lentz has lived in Killingworth, he has restored an 18th-century house, helped found the town historical society and served on the land trust and planning and zoning commission. He recently published a softcover book with more than 200 historical photographs of the town.



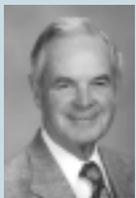
ISABEL CHENOWETH

The history of his department and of the School of Medicine itself is palpable in Lentz’s office. He rescued from the garbage the chair he offers to visitors. It belonged to Thomas R. Forbes, PH.D., who came to Yale in 1945. Forbes eventually became the Ebenezer K. Hunt Professor of Anatomy and chaired the admissions committee throughout the 1950s and 1960s. Lentz had sat in that chair for his own admissions interview. It gives him a good deal of pleasure to offer the chair to accomplished hopefuls today. “They inspire me,” he said.

—Colleen Shaddox

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.



John Ferguson



Howard Koh



Andrew Newman



Patrick Charmel



Jonathon Lewin



Edward Tyau



Michelle Dequina

1930s

John P. Ferguson, M.D. '39, dropped us a note recently, recalling that he "won the Yale Golf Championship in the year 1934-35. Now I've found out they don't make the balls as good as they used to. They don't go as far!"

1960s

John J. Schrogie, M.D. '60, vice president for periapproval and geriatric research studies at Omnicare Clinical Research in King of Prussia, Pa., has received the 2005 Henry W. Elliott Distinguished Service Award from the American Society for Clinical Pharmacology and Therapeutics.

Donald G. Skinner, M.D. '64, received the 2005 Presidential Medallion in March from the University of Southern California (USC), where he is professor and chair of the Catherine and Joseph Aresty Department of Urology and holds the Hanson-White Chair in Medical Research at the Keck School of Medicine of USC.

1970s

C. Gene Cayten, M.D., M.P.H. '72, professor of surgery, community and preventive medicine at New York Medical College, has been appointed senior associate dean of Our Lady of Mercy Medical Center in the Bronx. At the college he has served as director and senior advisor of the Institute for Trauma and Emergency Care and was program director of the college's surgical residency programs at Our Lady of Mercy and Lincoln Hospital.

Howard K. Koh, M.D. '77, has been named the first recipient of the Harvey V. Fineberg Professorship of Public Health at the Harvard School of Public Health. The chair honors a former dean of the school. Koh previously served as Massachusetts' commissioner of public health.

Pamela H. Nagami, M.D. '76, of the Kaiser Permanente Woodland Hills Medical Center, was one of 12 physicians to receive the Southern California Permanente Medical Group 2004 Physicians' Exceptional Contribution Award. The award recognizes physicians who have made noteworthy contributions to their communities.

Andrew B. Newman, M.D. '75, is the chair and managing director of the newly founded Ocean Medicine Foundation in California. He will maintain his pulmonary practice and adjunct clinical faculty position at Stanford while working with the foundation to improve the health of people on islands by increasing the quality of island-based health care and ocean science and by preventing the global spread of epidemics.

1980s

Patrick A. Charmel, M.P.H. '83, has been appointed to the National Advisory Council for Healthcare Research and Quality, which advises the U.S. Department of Health and Human Services and its Agency for Healthcare Research and Quality. Charmel is president and CEO of Griffin Hospital and its parent company, Griffin Health Services Corp., in Derby, Conn.

Jonathon S. Lewin, M.D. '85, HS '86, a neuroradiologist with a research interest in MRI-guided interventional procedures, was named the Martin W. Donner Professor and director of the Department of Radiology at Johns Hopkins. He and his wife, Linda O. Lewin, M.D. '87, and their children live in Baltimore, Md.

James S. Marks, M.D., M.P.H. '80, has been named senior vice president and director of the health group of the Robert Wood Johnson Foundation. He is the former acting director of the Coordinating Center for Health Information and Service at the Centers for Disease Control and Prevention.

Edward S. Tyau, M.D. '85, of the Kaiser Permanente Riverside Medical Center, was one of 12 physicians to receive the Southern California Permanente Medical Group 2004 Physicians' Exceptional Contribution Award. The award recognizes physicians who have made noteworthy contributions to their communities.

1990s

Senda Benaissa, M.P.H. '95, was married to Mario Hernandez in October. Benaissa is a research scientist at Gallaudet Research Institute and consultant at the World Bank in Washington, D.C., focusing on health care and international disability.

Mark Coyle, PA '96, and Stacey L. Frasca, PA, were married on September 12. Both the bride and groom work as physician assistants at St. Vincent Hospital at Worcester (Mass.) Medical Center.

Michelle P. Dequina, M.P.H. '98, currently studying for her M.B.A. at Yale, and Neal K. Nakra, M.D., a fellow in pediatric pulmonology at Yale-New Haven Hospital, were married on January 14.

Manendiu A. Ndoping, M.P.H. '98, a manager at the Health Strategies Consultancy in Washington, D.C., and Reginald P. Bazile, a consultant in Washington, were married on December 30.

Cynthia Carver Smith, M.P.H. '90, writes to say that she and her husband, Lt. Col. David B. Smith, USMC (Ret.), celebrated their fourth wedding anniversary last September. David is an IT executive for the Securities and Exchange Commission, and Cynthia owns a telecommunications company in the Washington, D.C., area. In 1999 Cynthia and David founded Cynthia's Kids, a nonprofit devoted to the well-being of children, and they recently made a gift to Yale School of Medicine's Department of Obstetrics, Gynecology and Reproductive Services in memory of their twins, Jack and Julia Smith.

2000s

Aviv Halpert, PA '01, a pediatric physician assistant at Montefiore Medical Center in New York, was married to Jessica Pitt, a pediatric occupational therapist, on November 26, 2003.

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

VISIT US ON THE WEB
yalemedicine.yale.edu

Elisha Atkins, M.D., professor emeritus of medicine, died on April 22 at the age of 84 in Belmont, Mass. With Yale colleague Phyllis Bodel, M.D., Atkins demonstrated the close relationship between the induction of fever and the ability to resist infection, and was author of numerous research articles on fever and infection. At the School of Medicine, Atkins served on the admissions committee and for a year was acting associate dean. He also served as master of Saybrook College, one of Yale's undergraduate residential colleges.

John E. Bowers, M.D. '47, died on February 10 at the age of 80. Bowers was a lieutenant in the U.S. Navy during the Korean War and was the chief of staff at Plantation General Hospital in Plantation, Fla.

Sonja M. Buckley, M.D., a Yale virologist who in 1969 helped to identify the deadly Lassa virus, which originated in Africa, died on February 2 in Baltimore at the age of 86. Buckley received her medical degree from the University of Zurich in 1944. After coming to the United States, she worked first as a research assistant at John Hopkins, then at the Sloan-Kettering Institute, where she became head of the solid tumor program in 1949. She began working on viruses at the Rockefeller Foundation in 1957 and came to Yale in 1964. She retired in 1994.

Marshall Edelson, M.D., PH.D., died at the age of 76 on January 16 in Woodbridge, Conn. Edelson was a professor emeritus of psychiatry at the School of Medicine, where he taught for over 30 years. He wrote nine books on topics ranging from group therapy to psychoanalytic theory and received many awards for his teaching and scholarship.

Nicholas M. Greene, M.D., founder of the Department of Anesthesiology at Yale, died in New Haven on December 28 at the age of 82. Greene, one of the founding fathers of modern anesthesiology, served as director and chair of the department for 18 years. He is credited with transforming the service at Yale from a technical subspecialty of surgery into a medical and academic discipline in its own right. He published several books and more than 200 articles about education and the physiological changes associated with anesthesia. In 2001 the School of Medicine honored Greene with the establishment of the Nicholas M. Greene Professorship in Anesthesiology, an endowed chair.

William E. Laupus, M.D. '45, died on February 14. Laupus taught at New York Hospital before going into private practice in Detroit. He returned to teaching at the Medical College of Georgia, Augusta, as assistant professor of pediatrics, and then became chair of the department of pediatrics at the Medical College of Virginia in Richmond. As founding dean, he transformed the School of Medicine at East Carolina University, Greenville, N.C., into an accredited four-year program.

James M. Malloy, M.P.H. '67, died on January 27. After his graduation Malloy worked for Yale University and then Waterbury Hospital. He also served as the CEO of three medical centers before moving to Jackson, Miss., where he founded one of the state's first HMOs. He subsequently started a health care consulting practice. Malloy raised money for health care initiatives serving underinsured communities in Mississippi, earning him the Distinguished Alumni Service Award from the School of Public Health in 2004.

Yvedt L. Matory, M.D. '81, died on April 15 in Needham, Mass., of complications from melanoma. She was 48. Matory was an associate surgeon in the Division of Surgical Oncology and co-chair of the Women's Cancer Program at Brigham and Women's Hospital in Boston. In 2000 she started HospitalCareOnline, a company that uses computers and remote monitoring to care for patients after their discharge from the hospital.

Eric W. Mood, M.P.H. '43, died on December 31. Mood was a veteran of World War II, who served in Italy and the South Pacific. He retired from the Army Reserve as a colonel. He worked as director of the Bureau of Environmental Sanitation for the New Haven Health Department before joining the Yale public health faculty as a lecturer. In the mid-1960s he developed the Division of Environmental Health and served as its director. His research focused on food sanitation, waste water treatment, swimming pool standards, drinking water quality, air pollution and the health aspects of housing.

Alvin Novick, M.D., professor of ecology and evolutionary biology, died in New Haven of prostate cancer on April 10 at the age of 79. After serving in World War II, during which he was a prisoner of war in Germany, Novick studied medicine at Harvard. He taught biology at Yale for 48 years and was a world-renowned expert on bat echolocation. Starting in 1982, however, he turned his attention to the AIDS crisis. He was chair of the Mayor's Task Force on AIDS in New Haven and a founder of AIDS Project New Haven and Leeway, Connecticut's only nursing home for the treatment of people living with AIDS.

George A. Silver, M.D., died on January 7 at the age of 91 in Chevy Chase, Md. A professor emeritus of public health at Yale, Silver served as deputy assistant secretary for health and scientific affairs at the U.S. Department of Health, Education and Welfare from 1965 until 1968. He served in the Army Medical Corps in Europe during World War II, helping to liberate Dachau and other concentration camps. After the war, he was chief of the social medicine division at Montefiore Hospital in New York. He served on the World Health Organization's expert committee on medical care and was secretary of the Federation of American Scientists' national council.

SEND OBITUARY NOTICES TO

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Antibiotic-resistant ribosomes unmasked

Five years ago, Yale scientists made a splash with the long-sought atomic structure of the large subunit of the ribosome, the protein-synthesizing factory of the cell and a target for many antibiotics (See “Yale Researchers Solve Structure of the Ribosome,” Fall 2000/ Winter 2001). It was the largest asymmetric structure to be solved up to that time, and the work, coming from the laboratories of Thomas A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry and a Howard Hughes Medical Institute investigator, and Peter B. Moore, PH.D., Sterling Professor of Chemistry and professor of molecular biophysics and biochemistry, settled many long-standing questions about protein synthesis.

This spring the Yale group offered a new collection of structures that explain how some bacteria escape the killing effects of some antibiotics. With antibiotic resistance threatening to undo years of progress against infectious disease, the work provides a road map to new antimicrobial drugs.

Many commonly used antibiotics bind to the same large pocket in the bacterial ribosome and block its ability to synthesize proteins. In a study published in the April 22 issue of the journal *Cell*, Steitz and Moore investigated how azithromycin and four other antibiotics bind to the ribosome in drug-resistant and nonresistant bacteria. All are affected by the same crucial change in just one of the 3,000-plus RNA nucleotides that make up the large subunit.

“We found that mutations creating resistance result in the insertion of one extra polar bump into the drug binding site that pushes a bound drug a little further away from its preferred position than it would like to be,” said Moore. “The shape and charge complementarity go from nice to not quite so nice, and you go from sensitive to resistant because the amount of drug it now takes to inhibit these bacteria is more than patients can tolerate.”

Knowing the problem suggests its solution—redesign antibiotics so they can fit around the bump. Now researchers can exploit structure-based drug design, a technique that has yielded successful treatments for AIDS and cancer. That effort will continue close to home, at Rib-X Pharmaceuticals, the New Haven startup that Steitz, Moore and several Yale colleagues co-founded back in 2001, in the wake of solving their first ribosome structure.

—Pat McCaffrey



OCTOBER 1955

Alumni Bulletin

New Graduate Program in Medical Sociology

“Yale University will start a new graduate program in medical sociology—the first of its kind in the nation to train students to apply the knowledge and techniques of sociology to the fields of medicine and public health. The new program will attempt to bridge the gap between medicine and sociology—between the doctor and the society which he serves. It will prepare students for teaching, research and administrative positions involving the social aspects of health and medicine. ...

“The first year will be spent in courses designed to meet special interests and training needs. The student will study the application of medical knowledge to public health problems, as well as the relationship of public health to various sociological phenomena. Courses will be taken in both the Department of Sociology and the School of Medicine. The second year of the program will be devoted to a thesis in the field of health or medical problems and society.”



WINTER / SPRING 1980

Yale Medicine

Match Day 1980

“Match Day is the culmination of several months of planning, counseling, and decision making on the part of senior medical students, deans and faculty, as well as hospitals participating in the National Resident Matching Program (NRMP). The program was developed during the 1950s when there were more internship positions available than there were medical school graduates to fill them. As a result, many hospitals were exerting pressure on students to sign contracts for their internships early in their senior year; some even pressed for decisions early in the sophomore or junior years. In 1953, after several attempts to establish an equitable system for internship appointments, the basic rules of the existing NRMP were set. ...

“This year, March 12 was Match Day. At Yale, of the 96 members of the Class of 1980, 42 students received appointments to the hospital of their first choice; 19 were appointed to the hospital they listed as second choice; and 10 to their third choice.”

AFTER 18 YEARS, A FAREWELL TO YALE

Visitors to the Office of Alumni Affairs will still be able to help themselves to a donut or some candy from the ever-present dish by the door. But the cheery smile and boundless enthusiasm Sharon R. McManus brought to her job as director of alumni affairs, a post she assumed in 2000, will be absent. (Not to mention the Irish soda bread she brought each year on St. Patrick's Day.)

Alumni around the country got to know McManus during her frequent trips organizing receptions and meetings, as well as at the annual reunion where she was, as office administrator Patricia DiNatale said, the "ambassador of smiles." In addition to planning and overseeing the annual reunion, McManus launched a Web-based program to enlist alumni as mentors for current students, especially during the residency application process.

After 18 years at Yale, including 16 at the School of Medicine, McManus left in May to join the staff of the Nightingale-Bamford School, a K-12 school for girls in New York City.

At a farewell party in early May, an ode to McManus written by a colleague recalled her "smiling face, that sweet Irish laughter ... For all who visit alumni affairs, you're engulfed with the feeling someone truly cares!"



JOHN CURTIS

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summer 2005

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