

Yale Medicine

winter 2002



Kenya Airways
NAME *K. Schmidt*
ADDRESS *P.O. Box 76634*
COUNTRY *Nairobi Kenya*
PHONE *254-2-57071*
KA (141 - LAB - 32400)

Letter from Nairobi



Comic Book Series!

NURU

Should I show her my TRUE feelings?



Bruce

Oscar
It's HIS life to live- does he know it?



Leon
He THINKS he's so cool-but what does cool really get you?



Janet
Too much, too soon?



Beverly Wilson Jr.

Confronted by CHALLENGES, will Nuru make the right CHOICES?



Angelina
Too loose. So LOST.

Should I tell Oscar the TRUTH?



Oscar's Uncle

Sugar Daddy
It's HIS game... who wins?



Mwalimu Tabu
His marks may COST you!!

WINTER 2002

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

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

- The Historical Library's online exhibit about the School of Medicine's last half-century
 - A longer discussion of the *Lessons from Anthrax* roundtable
 - More photos from the White Jacket Ceremony, Hunger and Homelessness Auction and the annual symposium of the Committee on International Health
- On the website, readers can submit class notes or a change of address, arrange for a life-long Yale e-mail alias through the virtual Yale Station, check the alumni events calendar and search our electronic archive.

ON THE COVER

A two-year assignment in Kenya's capital gives a recent public health graduate a chance to make a difference in the effort to contain AIDS. "In the two years I'll spend here, I can't really expect to see a noticeable change in the HIV incidence rate, and even if I did I would be hard pressed to say I had contributed to it," writes Karen Schmidt. But, she adds: "I have to believe that every little bit helps." Page 16

Cover collage by Janis Melone; AIDS prevention poster (left) by Bella Kilonzo/Program for Appropriate Technology in Health, Nairobi

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By Karen Schmidt, M.P.H. '00

24 LESSONS FROM ANTHRAX

The deaths of five people exposed to anthrax this fall put bioterrorism squarely on the map. Where does the road lead from here?

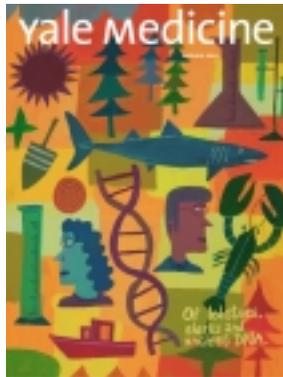
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By Marc Wortman

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CHALLENGE FOR THE EYES, EVEN YOUNG ONES

I received the new *Yale Medicine* [Autumn 2001] yesterday, and the new format is nice. I would like to say, however, that the type is a little small. It is bad enough for me, a member of the Class of 2000. I can only imagine how blurry it must appear for your alumni who have lost the ability to accommodate.

JOHN MAHONEY, M.D. '00
FALLS CHURCH, VA.

A CLASSMATE REMEMBERED, NEARLY FORTY YEARS LATER

I remember Donald Cohen [*In memoriam*, Autumn 2001].

I recall our first meeting. September 1962. By the democracy of the alphabet, Donald and I were teamed for the first year on that special experience, our own corpse. We got on well. Donald was serious, but with dry humor. It came out that he was quietly religious, but took his Judaism with reservations and gentle banter. I had waved goodbye to the Pope a long

time ago. Donald gave a shrug (he was good at shrugging) and never tried to sell me his package.

From day one, Donald was interested in psychiatry, especially child psychiatry. I had a flirtation with shrinkery, and there was an informal student interest group, where we further met. The psychiatry department was then heavily into psychoanalysis; I decided I did not need more religion.

In our final year as students, we met again on a general surgery rotation. Our resident, Nicholas Passarelli, M.D. '59, was really cool and sharp. Dr. Nick immediately realized Donald and I did not have the "right stuff" to be surgeons, but as long as we worked hard and did not sass, we got along fine. For some reason we all decided, in that era of overhead paging, that Dr. Nick needed two Irish assistants. And for six weeks Don Cohen was "Dr. Quinn."

Like some 19th-century cavalryman in Austria-Hungary, I drifted to the fringes of empire, never to be heard from; remembered only by the alumni fund. Donald returned to the citadel in New Haven. Periodically, I saw mention of his work and growing academic rank. It gave a measure of reflected glory, for once we had been students in medicine and young, in rites of passage, together.

We met briefly at class reunions. To my surprise, he was not at Reunion 35 earlier this year. His final illness explains the lapse.

Tomorrow I go on a long auto trip. The audio book *Swann's Way* from *Remembrance of Things Past* goes with me. I shall remember Donald and things past...

EUGENE CASSIDY, M.D. '66, HS '68, FW '70
MARSHALLTOWN, IOWA

A REMINDER OF WORDS FROM NOT SO LONG AGO

Though tired after replacing a hip and intertrochanteric fracture that afternoon and evening, I was surprised to see an excerpt from my long-ago article—*An African Summer*—in the Winter 1966 issue of *Yale Medicine*. My only concern was seeing the article being carried in the *Archives* section [Autumn 2001]. Instead of an excerpt from my article, I was expecting something from the 1740s.

But I'm flattered just the same.

Your fellow archivist,

ROBERT L. MCROBERTS, M.D. '66
ALBUQUERQUE, N.M.

HOW TO REACH US

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

FROM THE EDITOR

New paths, new knowledge

Ten years ago, when I was editing Karen Schmidt's articles at the daily newspaper where we both worked, I wouldn't have guessed that someday I'd be fielding her dispatches from Africa. But life's events brought me to Yale as an editor in 1994, and a few years later Karen enrolled as a master's degree candidate here at the School of Public Health. Now she is living in Kenya and working for a nonprofit organization devoted to *aids* prevention.

As her career has shifted full-speed into international health, Karen has retained her reporter's eye; she has both a knack for quick-sighted observations and a gift for articulating them with style and a sense of humor. Her cover story—the second in the “Letter from ...” series that debuted last spring with Sharon Chekijian's report from Armenia—offers a glimpse of life in a major African city and a look at the challenges facing health professionals trying to stem the global advance of *hiv*.

Also probing unexplored territory this issue are the Yale scientists pushing the boundaries of microarray technology in search of new therapies [“Targeting Cancer by Subtype,” page 28], as well as the alumni and faculty experts who are wrestling with the threat of bioterrorism [“Lessons from Anthrax,” page 24]. As with Karen, their sense of intellectual adventure has led them down new paths. All three areas of inquiry promise to make a lasting contribution to medicine and public health around the world.

Michael Fitzsosa
michael.fitzsosa@yale.edu

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Editor-in-Chief

Michael Kashgarian, M.D.
Professor of Pathology and Biology

Publisher

Jane E. Reynolds
Associate Dean

Editor

Michael Fitzsosa
Director of Publications

Associate Editor

John Curtis

Contributing Editors

Sharon McManus
Karen Peart
Cathy Shuffro
Jacqueline Weaver
Marc Wortman, Ph.D.

Contributors

Anna Carew-Miller
Karen Schmidt
Pem McNerney

Copy Editing

Anne Sommer

Office Manager / Editorial Assistant

Claire M. Bessinger

Senior Administrative Assistant

Cheryl R. Violante

Design

Daphne Geismar

Typesetting

Amy Storm

Design Consultant

Peter Johnson
Yale RIS Graphic Design

Production Consultant

Joe Maynard
Yale RIS

Printing

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Address correspondence to:

Editor, *Yale Medicine*
P.O. Box 7612
New Haven, CT 06519-0612
Telephone: 203-785-5824
Facsimile: 203-785-4327
Electronic mail: ymm@yale.edu
Website: <http://info.med.yale.edu/ymm>

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JOHN CURTIS (2)

By mid-January, the exterior of the Congress Avenue Building was largely finished and the project was slightly ahead of schedule. A café opened at the end of January, joining the new Yale Medical Bookstore (photo below right) in retail space across the street.

MEDICAL SCHOOL SHOWS A CHANGING FACE

As the Congress Avenue Building nears completion, a flurry of smaller projects alters the campus scene.

Before suburbs lured people from cities and Route 34 drove a wedge through downtown New Haven, the neighborhood surrounding the medical school bustled with businesses, shops and restaurants. In recent years, however, campus buildings have offered a stern face to the outside world, uninviting to those not practicing or studying medicine or seeking medical attention.

Now, as a number of construction projects near completion, the medical school campus is undergoing a major facelift. At the corner of Cedar Street and Congress Avenue, buildings which for years were open only to those bearing a Yale or hospital ID now include two stores catering to the public—the Yale Medical Bookstore and Cappuccino's & More, a gourmet coffee shop.

"With the opening of the Congress Avenue Building [*cab*], the school's center of gravity will start to shift down Cedar Street," said Irwin M. Birnbaum, *j.d.*, the medical school's chief operating officer. The corner of Cedar and Congress, he added, "is a place that is convenient to all. By adding a bookstore and coffee shop we are recognizing the importance of having facilities near the *cab* that will be more convenient for our staff there."

Cappuccino's & More, which opened in January, has seating for 32 with counter and takeout service. The Yale Medical Bookstore, affiliated with the Barnes & Noble bookstore on Broadway in New Haven, opened in October to

replace the Yale Co-op's medical branch on York Street, which closed last year. The bookstore caters largely to medical students and professionals, but manager Don Levy said many patients come straight from doctor's visits to look for books describing their ailments. Also available are stethoscopes, tuning forks, scrubs and study guides.

Among the major projects under way:

- At the site of the 457,000-square-foot Congress Avenue Building, scheduled to open in March 2003, workers have enclosed the building and begun to install plumbing, electrical wiring, *hvac*, partitions, shelves, benches and other laboratory casework.
- At the end of the B wing in the Sterling Hall of Medicine (*shh*), construction began in March 2001 on the Center for Drug Discovery, a three-story addition that will provide 25,000 gross square feet of wet-bench laboratory, laboratory support and office space. Renovations to the B wing will provide an additional 24,000 square feet of upgraded office, laboratory and support space for the Department of Pharmacology.
- A full renovation of the second floor of the C wing, home to cell biology in *shh*, began in October and is scheduled for completion in August. About 15,000 square feet will be reorganized into four laboratory modules, along with faculty offices and laboratory support spaces.
- Construction is under way at the corner of Amistad and Cedar streets on a 110,000-square-foot building and garage, with six floors devoted to disease-based clinical services and 950 parking spaces.



WITH DIRECTOR'S PASSING, CHILD STUDY CENTER FINDS ITSELF AT A CROSSROADS

In 1972, Albert J. Solnit, *m.d.*, *hs* '52, Seymour L. Lustman, *ph.d.*, *m.d.*, *hs* '57, *fw* '58, and Edward F. Zigler, *ph.d.*, sat down with a recent graduate of the School of Medicine and made a pitch for him to return to Yale to join the faculty. Solnit was then director of the Yale Child Study Center, Lustman was a professor, and Zigler, a founder of the Head Start Program, was returning to Yale after two years as head of the federal Office of Child Development and U.S. Children's Bureau.

The new recruit was Donald J. Cohen, *m.d.* '66, who accepted the offer and moved his young family to New Haven from Washington, where he had been Zigler's special assistant. Cohen was the kind of scholar that Solnit, Zigler and Lustman thought would thrive in the rich intellectual setting of the Child Study Center. "Donald had a brilliant understanding of the biochemistry and genetics of child development, and at the same time he was becoming a psychoanalyst and a talented child psychiatrist," recalled Solnit. Cohen, who succeeded Solnit to become the center's fourth director in 1983, went on to build it into an academic and clinical powerhouse with special strengths in the research and treatment of autism, obsessive-compulsive disorder and Tourette's syndrome, the psychological problems of children exposed to violence, and the developmental disorders of early childhood.

Cohen died October 2 at the age of 61, less than two years after being diagnosed with ocular melanoma. "His death was tragic and it was horribly premature. As a healer, as a scientist and as a leader, he is not a person who can be replaced," said Dean David A. Kessler, *m.d.* Yet during the months and years before his death, Cohen did much to pave the way for his own successor through recruitment and fundraising, according to James F. Leckman, *m.d.*, the center's director of research



JOHN CURTIS

Donald Cohen left the Child Study Center in excellent condition, colleagues say. Above, the center's Irving and Neison Harris Building addition, which opened in 1999.

and Neison Harris Professor. "Donald left us in really superb condition."

Kessler said it is likely that a new director will be named early this year.

The Child Study Center traces its roots to 1911, when Arnold Gesell, *ph.d.*, *m.d.* '15, established what would become the Yale Child Development Clinic. It was renamed the Child Study Center in 1948 with the arrival of the second director, Milton J.E. Senn, *m.d.* (See photograph, page 14), who recruited Solnit and others interested in child psychoanalysis and the role emotions play in healthy development. When Solnit became director in 1966, he began applying knowledge of child development to aspects of childhood that had been considered beyond the sphere of medicine. The center created a network of nursery schools and, through the work of Zigler and James P. Comer, *m.d.*, *hs* '66, began exploring ways to work with school systems to enrich the lives of children beyond academics. Solnit also established programs to help children in the juvenile justice system.

During his years as director, Cohen not only created vigorous research and clinical programs but also became skilled at building the center's resources.

At the suggestion of Irving Harris, a Yale alumnus and benefactor, he formed the Associates of the Child Study Center, a national group of highly motivated volunteers that numbers 160 today. Harris and his brother Neison endowed five professorships and the center's recent 21,000-square-foot addition between Sterling Hall of Medicine and Harkness Dormitory. "Donald engaged the associates as our consultants and colleagues," said Linda C. Mayes, *m.d.*, the center's Arnold Gesell Professor. "Some of our finest work has come from those collaborations."

Maintaining the center's preeminence will be one of the challenges facing the next director, said Mayes. Another will be preserving the collegial environment of the center as it continues to grow. But perhaps most important for the next leader, said Solnit, will be making his or her own distinct imprint. "The blueprint that Donald set out will continue to maintain its momentum," he said, "but the new director will have to resist the temptation to try to be like Donald. The new director, as Donald himself was, will have to be his own person."

INSTRUMENT SHOP ENDURES AS A PLACE FOR REPAIRS, A CATALYST FOR CREATIVITY

Tucked into the basement of the Hope Building at the corner of Congress Avenue and Cedar Street is a warren of well-lit rooms filled with milling machines, table saws, welders and lathes—a place where a scientist in need can go for a centrifuge repair or a part for a pH meter. The Instrument Repair and Design Shop has catered to medical school researchers for more than three decades, building prototype devices for use in experiments and performing emergency repairs on equipment that fails.

It's a distinguished history that almost came to an end. According to faculty member Vinzenz M. Unger, *ph.d.*, the shop provides researchers with essential technology not commercially available elsewhere. Yet years of running in the red threatened the shop's existence, and in 2000 it appeared to be on its last legs.

That was before a hue and cry arose from faculty members who had come to appreciate the instrument shop not only as a provider of engineering services but also as a catalyst for intellectual creativity and innovation—something difficult to measure in terms of profitability.

Faculty advisors Robert H. LaMotte, *ph.d.*, and Kenneth R. Williams, *ph.d.*, worked with administrators and the shop engineers to find a solution. Shop engineers James F. Hogan and Eugene J. Modzelewski streamlined existing services, reconfigured the fee schedule and developed a marketing plan to increase the instrument shop's customer base.

Now, said Carol S. Marshall, the school's director of training and quality improvement, the shop is in the black for the first time in seven years. The key to balancing the books, she said, was increasing the shop's visibility and encouraging an entrepreneurial approach to the shop's business.

Hogan and Modzelewski perform many services, from such mundane tasks as ordering specialized plastics

and repairing Geiger counters to talking through experiments with researchers and planning the design and fabrication of delicate laboratory instruments. Hogan has been tinkering with designs for Yale researchers for 40 years, initially working with the Department of Surgery in the design of pacemakers before joining the instrument shop staff in 1985. Trained as an electrical engineer, he said that his real education has come on the job while listening to the needs of researchers.

One of their recent projects was a "heart phantom" developed for researchers in the Department of Internal Medicine, with six progressively smaller chambers of Plexiglas sitting one within the other. The distance between chambers simulates the thickness of the myocardium during a contraction, allowing researchers to take measurements critical to their work.

Hogan and Modzelewski took the project from a series of discussions and paper sketches to a model on the computer screen to the eight-inch Plexiglas prototype sitting on the table when a visitor toured the shop recently. Hogan lifted the heart phantom, demonstrated the way the top seals two outer chambers in a vacuum and pointed out how the four remaining inner chambers would fit inside each other. "It's like being an artist," Modzelewski agreed. "We see how the pieces of the problem connect the way an artist sees color, and it all comes together."



Engineers Eugene Modzelewski (left) and James Hogan see the pieces of a problem "the way an artist sees color."

OVERCOMING JITTERS OF 9/11, YALE CELEBRATES 300 YEARS AND A GLOBAL FUTURE

On September 11, when terror struck the nation and America's mood suddenly turned somber, less than a month remained in Yale's Tercentennial year. The final weekend in the University's 12-month observance of its 300th anniversary had been planned for October 5 and 6, two days of festive celebration and academic ceremony. But in the days that followed the attacks on the World Trade Center and Pentagon, University leaders debated the wisdom of staging the Tercentennial finale in the Yale Bowl. Was it safe? Was it appropriate? Would people come?

"Carry on," was the message President Richard C. Levin said he received from the Yale community, Levin told 30,000 people gathered in the Yale Bowl on October 5. The crowd had come for a multimedia spectacular featuring famous Yale alumni celebrating Yale's contribution to the nation and the world. With that, a 150-member orchestra played and a 200-member chorus, along with the audience, sang "America the Beautiful," and the celebration continued.

Security was dramatically tightened for events that included a pomp-filled Tercentennial Convocation on Cross Campus and a two-day symposium, "Democratic Vistas, Global Perspectives," with talks by Yale faculty members, law school graduate and former President Bill Clinton and former President of Mexico Ernesto Zedillo, who holds a doctorate in economics from Yale and serves as a University trustee.

With Yale emphasizing its role as a world university in its fourth century, the School of Medicine figured prominently throughout the Tercentennial year because of the growing awareness of the global nature of public health concerns and the enormous impact of medical research advances on individuals and societies. In President Levin's Tercentennial address at the convocation on October 5, he said, "Through the subjects and students we teach and the

educational and research collaborations we undertake abroad, we can advance greater understanding among the world's peoples. We can also contribute to the solution of problems that cannot be contained within national borders—such as the spread of disease.”

In his talk before 8,000 people gathered on Cross Campus the following day, Clinton noted the phenomenal improvements in health care and life expectancy made possible by biomedical advances. He contrasted that progress in the developed world with the abysmal health care and short life expectancy seen in underdeveloped nations, which result in the rapid spread of disease and political instability. That is why, he said, “Yale’s mission to build a truly global university is so very important” in this new century that will be marked by increasing interdependence among nations.

In his speech, President Levin noted Yale’s commitment to invest nearly \$1 billion in the coming decade in medicine, science and engineering facilities. “No investment,” he said, “... holds greater promise for the health and prosperity of the nation and the planet.” And as a result of world events, Yale’s course for its next century has never been more clearly tied to a global future.



In his Tercentennial address, President Levin stressed Yale’s role as an international university.

et cetera

FUNDING THE HUNT FOR PROTEINS

Yale scientists have received a \$15 million, five-year grant that will fund a search for key regulatory proteins in the human genome. The grant from the National Human Genome Research Institute will create the Center of Excellence in Genomic Science, to be headed by Michael Snyder, PH.D., professor and chair of molecular, cellular and developmental biology. “Much of the human genome is comprised of DNA whose function is not known,” Snyder said. “Our team’s methods will elucidate the functions of many of these regions for the first time, and as a result of these studies, we will emerge with a much more detailed understanding of the human genome and its regulation.” Other investigators at the center are Mark B. Gerstein, PH.D.; Richard P. Lifton, M.D., PH.D.; Perry L. Miller, M.D., PH.D.; and Sherman M. Weissman, M.D.

ENDOWMENT DEFIES SLUMP

While most other university endowments posted double-digit declines as the economy soured in 2000-2001, Yale’s endowment ended the fiscal year with a 9.2 percent return on its investments. Fund managers attributed the endowment’s performance to diversified asset allocation, strong active management and a value orientation. Last year’s increase boosted the total to \$10.7 billion. For the 10 years ending June 30, 2001, the endowment returned an annualized 18.3 percent. As the endowment has grown over the past decade, from \$2.6 billion, its contribution to the University’s revenues has doubled, now accounting for 28 percent of the total. Spending from the endowment in the current fiscal year is expected to reach \$405 million, a 20 percent increase over the prior fiscal year.

DISCOVERY CHANNEL TAPS YSM

When the breakthrough cancer drug Gleevec made headlines, Yale Cancer Center Director Vincent T. DeVita Jr., M.D., HS ’66, was on hand (and online) to share his perspective with Web surfers at discoveryhealth.com. When the threat of bioterrorism put the nation on edge, infectious disease expert Andre N. Sofair, M.D., M.P.H. ’97, HS ’90, weighed in with “10 Things You Need to Know About Anthrax.” Both pieces grew from a new partnership between Yale and the Discovery Health Channel, which will draw on expertise from throughout the medical school. Faculty will also contribute to four, hour-long television programs and to three online columns: “Family Matters,” “Cutting Edge Medicine” and “Views on Health News.” The first cable special, about ADHD, will air later this year.



FOR SOME PATIENTS, THE ENEMY IS ANEMIA

A link is found between low red blood count, high mortality among elderly cardiac patients.

Although clinicians have long been uncertain about the benefits of blood transfusions in patients with heart attacks, a study by Yale investigators has found that they significantly improve chances for survival.

“Our principal finding is that a low hematocrit on admission is associated with higher mortality rates in elderly heart attack patients,” said principal investigator Harlan M. Krumholz, *m.d.*, associate professor of medicine (cardiology) and epidemiology. “However, blood transfusions, when given to these patients, can significantly decrease their mortality risk. This is the first study to highlight the important link between anemia, blood transfusion and mortality among elderly patients hospitalized for a heart attack.”

Krumholz and researchers at Brown University Medical School, Yale’s Department of Epidemiology and Public Health and the Yale-New Haven Hospital Center for Outcomes Research and Evaluation conducted a retrospective study of 78,964 Medicare beneficiaries 65 years and older who were hospitalized with acute myocardial infarction. After categorizing patients on the basis of their hematocrit levels, the researchers then explored links between transfusions and 30-day mortality. “Surprisingly, we found that 43.4 percent of elderly patients hospitalized with a heart attack are anemic, or have a blood count below 39 percent, at the time of admission,” said co-author Saif S. Rathore, *m.p.h.*, a lecturer in the Department of Internal Medicine.

The study also found that the most severely anemic patients were twice as likely to die within 30 days as those who were not anemic. Despite the higher mortality risk, fewer than a quarter of the patients with clinically significant anemia received a blood transfusion.

“Our data indicate that blood transfusions provided to elderly anemic patients can significantly reduce their risk of short-term mortality,” said Krumholz. “Most promisingly, our data indicate that this benefit is observed in elderly patients with blood count levels as high as 33 percent, a higher level than previously considered by clinicians. These data are particularly compelling given the lack of clinical guidelines concerning hematocrit levels at which to transfuse elderly patients with heart disease.”

The study was published in the October 25 issue of *The New England Journal of Medicine*. In an editorial accompanying the study, Lawrence T. Goodnough, *m.d.*, and Richard G. Bach, *m.d.*, of the Washington University School of Medicine, underscored the importance of these findings. “For the first time, we have evidence that patients with a specific clinical presentation are affected adversely by the underuse of transfusion,” Goodnough and Bach wrote. Based on this research, they suggested “that hematocrit levels should be maintained above 33 percent in patients who present with acute myocardial infarction.”

“We certainly feel that our findings should result in a change in clinical practice,” said first author Wen-Chih Wu, *m.d.*, a teaching fellow in internal medicine (cardiology) at Brown University.



Nearly half of elderly patients admitted for a heart attack are anemic, according to a study in the October 25 issue of *The New England Journal of Medicine*. Harlan Krumholz (above) and colleagues also found that blood transfusions and higher hematocrit levels reduce the risk of short-term mortality.

MEAT THE CULPRITS

Eating one’s vegetables could help ward off a form of cancer that has been on the rise for the last quarter-century, according to a study by investigators at Yale and around the country. Since the mid-1970s the rate of adenocarcinomas of the esophagus and gastric cardia has increased by 300 percent. “We found that many nutrients in foods of animal origin are significantly associated with a risk of developing this class of cancers,” said lead author Susan T. Mayne, PH.D. They also found that certain plant-based nutrients, including dietary fiber, dietary beta-carotene, folic acid and vitamins C and B6, were associated with a lower risk. Harvey A. Risch, M.D., PH.D., was the principal investigator on the study, published in the October issue of *Cancer Epidemiology, Biomarkers & Prevention*.



DIGITAL VISION

et cetera

SEDATIVE LINKED TO DELIRIUM

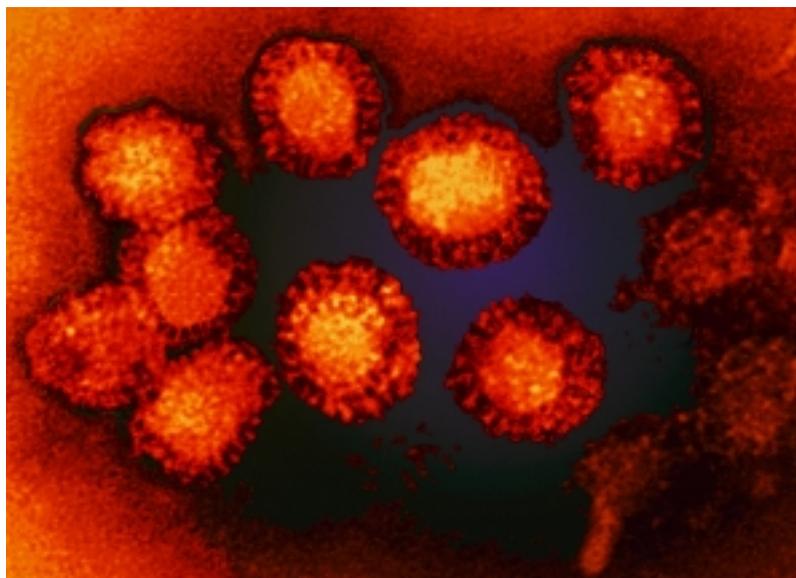
Older, hospitalized patients who take diphenhydramine, an often-prescribed anti-histamine and sedative, run a 70 percent greater risk of delirium, according to a study by Yale physicians. “The findings suggest that using diphenhydramine as a routine sleeping aid and for most other reasons should be actively discouraged in the older hospitalized population,” said Joseph V. Agostini, M.D., a postdoctoral fellow in the Robert Wood Johnson Clinical Scholars Program, whose findings were published in the September 24 issue of *Archives of Internal Medicine*. Diphenhydramine is a component of many over-the-counter cold remedies and allergy and insomnia medications such as Benadryl and Sominex.

ANOTHER APPROACH TO ADHD

The drug guanfacine can treat attention deficit hyperactivity disorder (ADHD) without worsening tics, Yale investigators have found. Stimulants are first-round agents for ADHD, but may worsen tics in some cases. “Guanfacine,” said first author Lawrence Scahill, M.S.N., M.P.H. '89, PH.D. '97, associate professor in the Child Study Center and at the School of Nursing, “appears to be a safe and effective treatment for children with tic disorders and ADHD.” For the study, published in the July issue of *The American Journal of Psychiatry*, the researchers followed 34 children diagnosed with ADHD and a tic disorder. Guanfacine was associated with improvement on the teacher-rated ADHD Rating Scale, fewer tics and better performance on laboratory tests of attention and impulse control.

LIFE AND DEATH ON THE GRIDIRON

This year across America, a handful of apparently healthy athletes will die on the playing field. Though efforts are made to detect abnormalities that might predict the sudden deaths resulting from hypertrophic cardiomyopathy and undiagnosed asthma, there has been no cost-effective way of screening entire teams before the start of each season. But last August, Yale surgeon James “Butch” Rosser, M.D., launched his “Operation Beating Heart” telemedicine program during football practice at Savannah State University in Georgia. Rosser’s exam uses a five-pound ultrasound device and other portable gear to transmit data to Yale physicians. Rosser plans to expand the program to other schools this year.



LINDA STANNARD/SCIENCE SOURCE/PHOTO RESEARCHERS

West Nile virus has led to about 10 deaths in the U.S. since it surfaced in New York in 1999.

A PROMISING VACCINE FOR WEST NILE VIRUS?

Engineered protein gives mice complete protection, could lead to a diagnostic test.

A vaccine developed by Yale scientists has protected mice from the West Nile virus, a mosquito-borne infection that has been linked to about 10 deaths in the United States since the summer of 1999.

The virus, first identified in Uganda in 1937, surfaced in the New York City area in 1999 and has subsequently appeared in the South and Midwest. It is considered an emerging disease, said Erol Fikrig, *m.d.*, associate professor of medicine and of epidemiology and public health. "Its seriousness as a public health threat is not fully known yet," said Fikrig, who directed the development of the vaccine. "That should become apparent over the next two to three years. If the vaccine proves necessary, its development will be valuable."

The virus, which infects birds as well as humans, spreads through mosquito bites primarily in warm-weather months. There is currently no cure, although infection does not generally cause seri-

ous consequences. Elderly patients, however, can develop fatal encephalitis, a central nervous system infection.

Fikrig and colleagues, including Tian Wang, *ph.d.*, a postdoctoral fellow in his laboratory, and John F. Anderson, *ph.d.*, research associate in epidemiology, and associates from the Connecticut Agricultural Experiment Station in New Haven, isolated a sample of the virus found in an infected bird. They genetically engineered a protein in the virus, which they then injected into uninfected mice. Immunization with the vaccine provided complete protection for the mice against West Nile virus.

Because diagnosis of West Nile virus can be difficult using current methods, the protein used to make the vaccine could also be employed to develop a diagnostic test, Fikrig said.

Results of the study were published online in the *Journal of Immunology* on October 23 and appeared in the November 1 print issue.

MOLECULE THAT TARGETS TISSUE FACTOR IS FOUND TO THWART TUMORS IN MICE

Yale researchers have developed a molecule that, when injected into tumors in mice, destroyed blood vessels in tumors and left normal tissue unharmed. Their findings, published in the October 9 issue of *Proceedings of the National Academy of Sciences*, hold the promise of a new therapy for metastatic cancer.

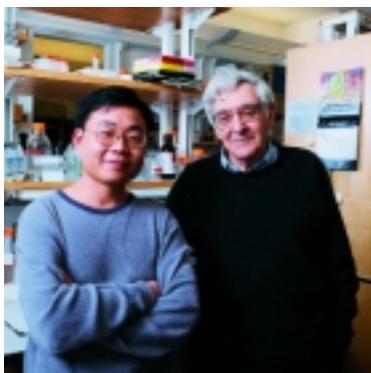
The molecule, developed by Alan Garen, *ph.d.*, and Zhiwei Hu, *ph.d.*, in the Department of Molecular Biophysics and Biochemistry, is an immunoconjugate, or icon, which joins elements of different molecules. The team's strategy—targeting a tumor's blood vessels without harming normal cells—led them to the molecule tissue factor (TF), which is expressed on the inner surface of the tumor blood vessels and initiates blood clotting.

Garen and Hu's icon is made up of two elements, one that draws it to TF and another that initiates an immune response. The first element is factor VII, a molecule that circulates in the blood and binds to TF. Once factor VII has drawn the icon to TF in the tumor, the icon triggers its second element, the Fc region of a human antibody, which activates the immune system against cells that bind to the icon. A replication-incompetent adenoviral vector was used to deliver the gene encoding the icon to the tumor cells. The tumor, once infected, produces and secretes the icon into the blood, where it circulates throughout the body seeking tumor blood cells.

"The result," said Garen, "is that the tumor's blood vessels are destroyed by the immune system, and consequently, the tumor cells die because they lack a blood supply. Normal blood vessels survive because they do not express tissue factor and therefore do not bind to the icon."

Garen and Hu first generated human prostatic and melanoma tumors in mice, then injected the vector into one of the tumors. A control group of mice received a blank vector; those mice died within 63 days after tumors appeared on the skin.

In the mice that received the icon molecule, tumor cells were eliminated and the mice remained free of the disease for at least 194 days. They received their last injection of the vector on the experiment's 53rd day, suggesting that the molecule's effects are long-lasting. In addition, the icon acted against tumors that had not been injected with the vector, offering the possibility of a treatment for metastatic cancer patients. "This icon should work against all types of tumors that contain blood vessels," Garen said.



ROBERT LISAK

Zhiwei Hu and Alan Garen have created a chimeric molecule that makes tumors disappear in mice.

KNOCK-OUT STUDY SHOWS HOW SOME WHITE BLOOD CELLS REGULATE SKIN CANCER

A type of white blood cell that is found in the skin and assists in the body's immune response also helps prevent skin cancer, Yale researchers have found.

Gamma-delta T cells play a major role in local immunity and "are likely to be crucial to an early defense against skin cells that have recently transformed to a premalignant or malignant state," said Michael Girardi, *m.d.*, assistant professor of dermatology. Girardi, primary author of a paper on the findings published in *Science* in September, was part of a team that included colleagues at Guy's King's St. Thomas Medical College in London. The team genetically engineered mice that were incapable of producing gamma-delta T cells, then exposed the knock-out mice to three different models of skin cancer.

In one model, tumor cells were injected into the skin. In another, a carcinogen was injected into the skin. For the third, carcinogens were repeatedly painted onto the skin. This last model most closely resembles cancer

development in humans because it mimics repeated exposures that progress from a benign thickening of tissue to premalignant papilloma to carcinoma formation.

Girardi and his team found that, in all three models, the absence of gamma-delta T cells resulted in a higher level of skin cancer formation. In the third model, however, another type of T cell, alpha-beta, contributed to skin cancer development and progression. "There appears to be a yin-yang contribution by alpha-beta T cells to skin cancer, in that they can act in both the defense against and the promotion of carcinoma," Girardi said.

Gamma-delta T cells work by expressing a protein, NKG2d, which binds to a molecule that is expressed by tumor cells. Once the molecule, Rae-1, is engaged by the NKG2d protein, gamma-delta T cells can kill the tumor cell. Rae-1 is expressed only in skin cells that have been exposed to chemical carcinogens that stimulate the transition to cancer. "This is an initial and important distress signal to the local T cells, and to some other cells of the immune system, that things are wrong," Girardi said.

et cetera

ROUTE OF INFECTION

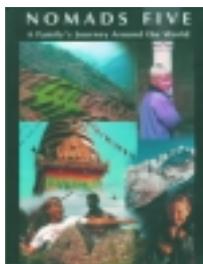
Investigators in microbial pathogenesis have described a secretion system that many bacteria—including those that cause plague, dysentery and typhoid—use to infect other cells. The type III secretion system found in *Salmonella* is a hollow, needle-like structure that delivers bacterial proteins into a host cell. "Many pathogens use a similar mechanism," said principal investigator Jorge E. Galan, *PH.D.*, chair of the Section of Microbial Pathogenesis, of the findings published in the November 1 issue of *Nature*. "Insight into any of them gives you insight into all of them. From this fundamental information we can begin to develop completely new therapeutic strategies to halt or prevent infections by these pathogens."

CROSSING OVER

Two Yale neuroscientists have discovered a pathway, apparently unique to humans, that guides neurons between different brain regions. "Disregarding boundaries between major brain divisions is unusual," said principal investigator Pasko Rakic, *M.D., PH.D.*, chair of the Department of Neurobiology and the Dorys McConnell Duberg Professor of Neuroscience, "and could explain how parts of the cerebral cortex associated with the highest cognitive functions may have coordinated their growth with subcortical structures during human brain evolution." Rakic and graduate student Kresimir Letinic found that attractive and repulsive molecules directed neuronal stem cells from the ganglionic eminence to the diencephalon. They published their findings in the September issue of *Nature Neuroscience*.

CLUES TO HOW A CELL MOVES

Using X-ray crystallography, investigators at Yale and the Salk Institute have solved the structure of Arp2/3, a complex of seven proteins that helps cells move. "Knowledge of the three-dimensional structure not only provides key insights about the Arp2/3 complex, but it will also elevate the level of research on cellular movements for years to come," said principal investigator Thomas D. Pollard, *PH.D.*, the Eugene Higgins Professor of Molecular, Cellular and Developmental Biology. The Arp2/3 complex initiates the assembly of the protein actin into filaments at the front end of a cell, which pushes the cell forward. The findings were published in the November 23 issue of *Science*.



Nomads Five: A Family's Journey Around the World

by Honey Sharp Lippman, Alexandra and Nadia Lippman, with contributions from David H. Lippman, *m.d.* '71 and Daniel Lippman

Eighty Days Press
(Great Barrington, Mass.) 2000

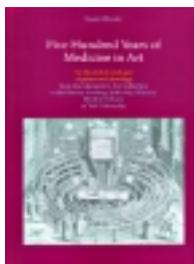
In 1995, for a 50th birthday sabbatical, David Lippman took his adventurous and tolerant wife and three children on a trip around the world. The book is the fruit of a decision to record the adventures this family experienced as it traveled over a nine-month period. While Lippman is not sure he would recommend extensive travel to a young family after the events of September 11, he hopes that our children can take their children on a once-in-a-lifetime trip which, for the Lippmans, brought them closer to each other and all their fellow travelers on our now-worried planet.

Five Hundred Years of Medicine in Art: An Illustrated Catalogue of Prints and Drawings from the Clements C. Fry Collection

edited by Susan Wheeler, curatorial consultant

Ashgate Publishing Co.
(Burlington, Vt.) 2001

This meticulously researched volume makes available an important collection of prints and drawings from the Cushing/ Whitney Medical Library at Yale and allows comparative study of specific medical themes as they have been portrayed over time by artists. The collection also reflects the professional interests of Fry, a Yale psychiatrist, bringing together many



works related to mental illness, including representations of patients, psychiatric institutions and therapeutic practice.

Handbook of Alcoholism

edited by Gerald Zernig, *m.d.*, Alois Saria, *ph.d.*, Martin Kurz, *m.d.*, and Stephanie S. O'Malley, *ph.d.*, professor of psychiatry

crc Press
(Boca Raton, Fla.) 2000

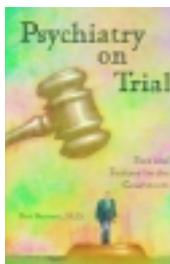
While the war on drugs continues to attract worldwide attention, the fact that alcoholism remains a major worldwide health concern is often overlooked. No matter what one's expertise, the *crc Handbook of Alcoholism* can help practitioners acquire the necessary skills to treat problem drinkers and alcohol-dependent patients. This comprehensive handbook addresses the underlying psychological problems of alcoholism, and helps practitioners to better diagnose and treat the nonpsychiatric medical disorders caused by the disease.

Psychiatry on Trial: Fact and Fantasy in the Courtroom

by Ben Bursten, *m.d.* '58, *hs* '62

McFarland & Company Inc.
(Je-erson, N.C.) 2001

In some areas of the law, psychiatrists have become as much a part of the legal landscape as lawyers and litigants. Psychiatrists' speculations garner criticism from both the medical and legal communities. In this work, the author takes a close look at psychiatric testimony and examines the validity of what forensic psychiatrists do. Using depositions from actual cases and



drawing from his own experiences, the author discusses the problem of misinformed professionals, appropriate and inappropriate testimony and the legal principles that help distinguish good testimony from bad testimony. Also covered are a wide variety of psychiatric and legal issues, including worker's compensation, murder, child abuse, repressed memory, malpractice and sexual harassment.

Beyond the Big Talk: Every Parent's Guide to Raising Sexually Healthy Teens—from Middle School to High School and Beyond

by Debra W. Haffner, *m.p.h.* '79

Newmarket Press
(New York) 2001

As children mature into potentially sexually active young adults, parents have an increasingly difficult time talking to them about the sensitive topics of sex and sexuality. The influences of the media, the Internet and peer pressure complicate relationships between parent and child and make it harder than ever before for parents to pass their own values on to their teens. But parents who are able to stay involved in their children's lives can make a big difference in the children's actions and behaviors.

Writing in a realistic, practical and informative style, Haffner provides a wealth of techniques and ideas for helping teens deal with sexuality issues. With checklists and sample conversations, she gives specific information particular to each age group: middle school, early high school, late high school and beyond. She addresses such crucial issues as peer pressure, dating and parties, alcohol and drugs, sexual harassment and abstinence.



Meselson, Stahl, and the Replication of DNA: A History of The Most Beautiful Experiment in Biology

by Frederic Lawrence Holmes, *ph.d.*, Avalon Professor and chair of the Department of the History of Medicine

Yale University Press
(New Haven) 2001

This book vividly reconstructs the complex route that led to the Meselson-Stahl experiment confirming that DNA replicates as predicted by Watson and Crick's double-helix structure. It also provides an inside view of day-to-day scientific research—its unpredictability, excitement, intellectual challenge and serendipitous windfalls, as well as its frustrations, unexpected diversions and chronic uncertainty. Holmes uses research logs, experimental films, correspondence and interviews with the participants to record the history of Meselson and Stahl's research, from their first thinking about the problem through the publication of their dramatic results. Holmes also reviews the scientific community's reception of the experiment, the experiment's influence on later investigations and the reasons for its reputation as an exceptionally beautiful experiment.

The descriptions above are taken from the book jackets.

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



SAMUEL O. THIER
Keeping values alive
in the marketplace

Most social institutions, according to Samuel O. Thier, M.D., former chair of the Department of Medicine and now CEO of the Harvard-affiliated Partners HealthCare, have failed to keep pace with the transition from the Industrial Age to the Information Age. “Medicine,” he said, “is perhaps as complicated as any social system we have. Doing anything to change it is going to create major problems.

“Nonetheless, if it continues to change in the fashion it is changing now, which is by chaos in the marketplace, without values driving that change, I fear for what might come out at the other end,” Thier said, as he delivered the Department of Medicine’s fifth annual Samuel O. Thier Lecture, named in his honor, on September 20.

Partners, founded in 1994 by Massachusetts General Hospital and Brigham and Women’s Hospital, has used the strength of its affiliations to preserve its values in an increasingly competitive marketplace. “Academic medicine,” Thier said, “provides not just the intellectual base, it provides social values, it provides education, it provides research, it advances care and it has been the safety net for the indigent and the people who are uncovered. The number of uninsured is still an embarrassment in this country. If those [academic] institutions are injured, then we have a major problem.”



GINA KOLATA
Getting it right for *The Times*,
and in a hurry

Journalists who cover medicine must do so under severe time constraints and often under pressure from people hoping to exact commercial or political profit, said Gina Kolata, a medical reporter at *The New York Times* who gave the first Margaret Roth-Glynn McKiernan Annual Lecture during dermatology grand rounds in September. Typically, she said, publicists swamp her with letters, e-mails, faxes and phone calls, all touting a real or perceived advance in medical care. “One of the things you start to ask yourself is, ‘What am I supposed to believe and how am I supposed to believe it?’” she said. Her skepticism about a press release promoting an exercise regimen led her to a physician who had lost his license in New York for fraud and mistreatment of patients. “The onus in medical reporting is really on the reporter. You have to get it right. Sometimes you have to get it right in a very short time. It’s an imperfect system. I don’t know if there’s a better one.”



MATTHEW MESELSON
“On the threshold of a
gigantic new technology”

“One can be sobered by the realization that virtually all the earlier technologies of our species—stonework, metallurgy, internal combustion, electronics—have been used for peaceful purposes, but all have also been exploited vigorously for hostile ones,” said Matthew Meselson, Ph.D., a microbiologist and expert in biological weapons. In a talk on October 23 sponsored by the Institute for Social and Policy Studies, “Averting Hostile Exploitation of Biotechnology,” he noted that with the unlocking of the human genome the stakes are even greater. “We are on the threshold of a gigantic new technology,” said Meselson, Cabot Professor of the Natural Sciences at Harvard. “It is totally different from all the previous technologies because it has the potential to change what it means to be human.” Controlling this new technology, he said, requires an international norm that would bar its hostile use.

Production and use of biological weapons, Meselson believes, should rank with aircraft hijacking and state-sponsored torture as an international crime with universal jurisdiction. He used the example of former Chilean president Augusto Pinochet, who was arrested in England after a judge in Spain filed charges against him for the torture of dissidents in Chile. “The development, production and use of biological weapons is the result of decisions made by individuals,” Meselson said. “Why not hold individuals responsible?”



JOHN CURTIS (4)

NILS DAULAIRE
With global health,
“There is no them, only us”

When anthrax scares put Americans on edge last fall, public health took center stage as a national security matter, said Nils Daulaire, M.D., M.P.H., the CEO of the Global Health Council, an organization that identifies and reports on world health problems. To be sure, noted Daulaire, health issues have always mattered in some security contexts, including the work of the CIA, which uses infant mortality rates as a measure of a country’s stability.

In a talk sponsored by the School of Medicine and the Department of Epidemiology and Public Health in October, “Fighting Terror with Hope: Global Health in the New Reality,” Daulaire placed post-September 11 health issues in a context of globalization, security and justice. “It is fundamentally unjust that a child born in Afghanistan has a chance of dying in childhood that is 30 times greater than that of a child born in Fairfield, Conn.,” he said of statistics that predate the bombing campaign that began October 7. “Focusing on global health is an appropriate rejoinder to what happened on September 11. It is something we need to do for the good of our own security. We need it for a global sense of justice. Ultimately, we need it for our souls. When it comes to global health, there is no them, there is only us.”

A half-century of growth

The medical school was a quiet place in 1951, with a part-time dean and only 23 full professors. What a difference 50 years makes.

by Pem McNerney



In 1911, Arnold Gesell inaugurated services for emotionally disturbed children as well as research into the normal development of children. These services, later known as the Yale Child Development Clinic, became renowned worldwide. When Gesell retired in 1948, the name was changed to the Child Study Center, which took a more environmental and psychoanalytic approach to child development. Milton Senn (above), a nationally prominent pediatrician, succeeded Gesell as director, serving until 1966.

In 1951, the School of Medicine operated on a budget of just over \$3 million. In 2001, annual revenue had grown 239-fold, to \$717 million.

In 1951, \$1 million was spent on research. Fifty years later, the total was 382 times that figure.

And at the century's midpoint, the medical school faculty counted only 23 full professors among its ranks. As of last October, that number had grown to 379, still just a fraction of the total 1,354 current full-time faculty.

It's fair to say that the school has grown dramatically over the past five decades.

That growth is the focus of *Medicine at Yale, 1951-2001*, the third in a series of exhibits at the Cushing/Whitney Medical Library curated by Historical Librarian Toby A. Appel, *ph.d.*, and Curatorial Consultant Lilli Sentz, *m.l.s.*, as part of the 300th anniversary celebration of Yale's founding in 1701.

The role of federal money in the expansion of the school was significant, and remains a considerable factor in the school's growth to this day. "After World War II, there were a number of agencies that got into funding science," said Appel. "During and after the war, the country's leadership decided that if you supported science, you would get breakthroughs, that there was a cause and effect." The increase in funding led to growth on several fronts, including the administration. Instead of just a part-time dean who taught on the side, the school eventually would have a full-time dean, assistant deans, associate deans and deputy deans.

The appointment of Vernon W. Lippard, *m.d.*, as dean in 1952 was significant because his full-time status allowed him to do a thorough job of

fund-raising, according to former Deputy Dean Arthur Ebbert, *m.d.*, who served on the faculty from 1953 to 1988 and provided assistance for the exhibit. Lippard launched several major building programs, said Ebbert, noting that the construction of Harkness Dormitory and Harkness Auditorium and the expansion of the Sterling Hall of Medicine took place during his deanship. During Lippard's tenure, the number of faculty more than doubled and the budget grew fivefold.

Like the rest of the country, Yale experienced considerable unrest during the 1960s. Fredrick C. Redlich, *m.d.*, dean from 1967 to 1972, led the school during the most turbulent years and oversaw the formation of five new departments and a 25 percent increase in the size of the faculty. Redlich strengthened basic science departments and grounded the teaching of psychiatry in the biological and behavioral sciences. He was succeeded by Lewis Thomas, *m.d.*, former dean at New York University and a noted pathologist and essayist, who left after a year to become the director of Memorial Sloan-Kettering Hospital in New York. His successor, Robert Berliner, *m.d.*, continued to build the school into a scientific powerhouse during his 11-year deanship, making it "one of the top two or three institutions in America in terms of hosting research supported by peer-reviewed grants," then-Yale President A. Bartlett Giamatti said upon Berliner's retirement.

Leon E. Rosenberg, *m.d.*, *hs* '63, dean from 1984 to 1991, oversaw the completion of the Boyer Center for Molecular Medicine, the Yale Psychiatric Institute, the Yale Physicians Building and the expansion of the Medical Library. He also helped raise \$155 mil-

lion to increase the endowment. Robert M. Donaldson, *m.d.*, led the school in 1991-92 until the arrival of Dean Gerard N. Burrow, *m.d.* '58, who returned to Yale after serving on the faculty of the University of Toronto and as dean and vice chancellor of the University of California San Diego. The exhibit credits Burrow with leading the School of Medicine through a difficult time of transition and promoting science and education despite threats of reduced external support.

The school's current dean, David A. Kessler, *m.d.*, was appointed in 1997 after serving for seven years as commissioner of the Food and Drug Administration. Kessler has presided over the continued growth of the school, shepherding construction of the Congress Avenue Building and a number of smaller building projects (See *Chronicle*, page 4). Speaking to a gathering of medical, nursing and public health alumni at the Yale Club of New York in January, Kessler said that the medical school will have added approximately 700,000 square feet of new or renovated space to its campus within several years and that the next 50 years may surpass the last half-century's growth. "I think," he said, "that we're in the greatest period of expansion in the medical school's history."

PEM MCNERNEY is a writer and editor with Content Creation Co. in Madison, Conn., and director of communications for the Center for Nicotine and Tobacco Use Research at Yale.

In 1952, Vernon Lippard (top right) became the first full-time chief administrator of the School of Medicine. Born in 1905, Lippard entered Yale College as a freshman in 1922. After three years of college, he was interviewed by then-Dean Milton Winternitz for admission to the medical school. The interview process was less formal at that time, and at the end of the interview, the dean told him: "All right, you can come." During Lippard's tenure as dean from 1952 to 1967, medicine at Yale experienced dramatic growth.



Vernon Lippard

CHARLES T. ALBURTUS

Under the chairmanship of Paul Beeson, the Department of Internal Medicine expanded from about 10 members in 1952 to nearly 100 in 1965. A noted specialist in infectious diseases, Beeson encouraged doctors to start their studies of disease at the bedside at a time when medical science was becoming increasingly laboratory oriented. In 1975, Beeson received an honorary doctor of science degree from Yale, and in 1996 the medical service here was named in his honor. A biography entitled *Physician: The Life of Paul Beeson* by Richard Rapport, *M.D.*, was published in 2001.



Paul Beeson

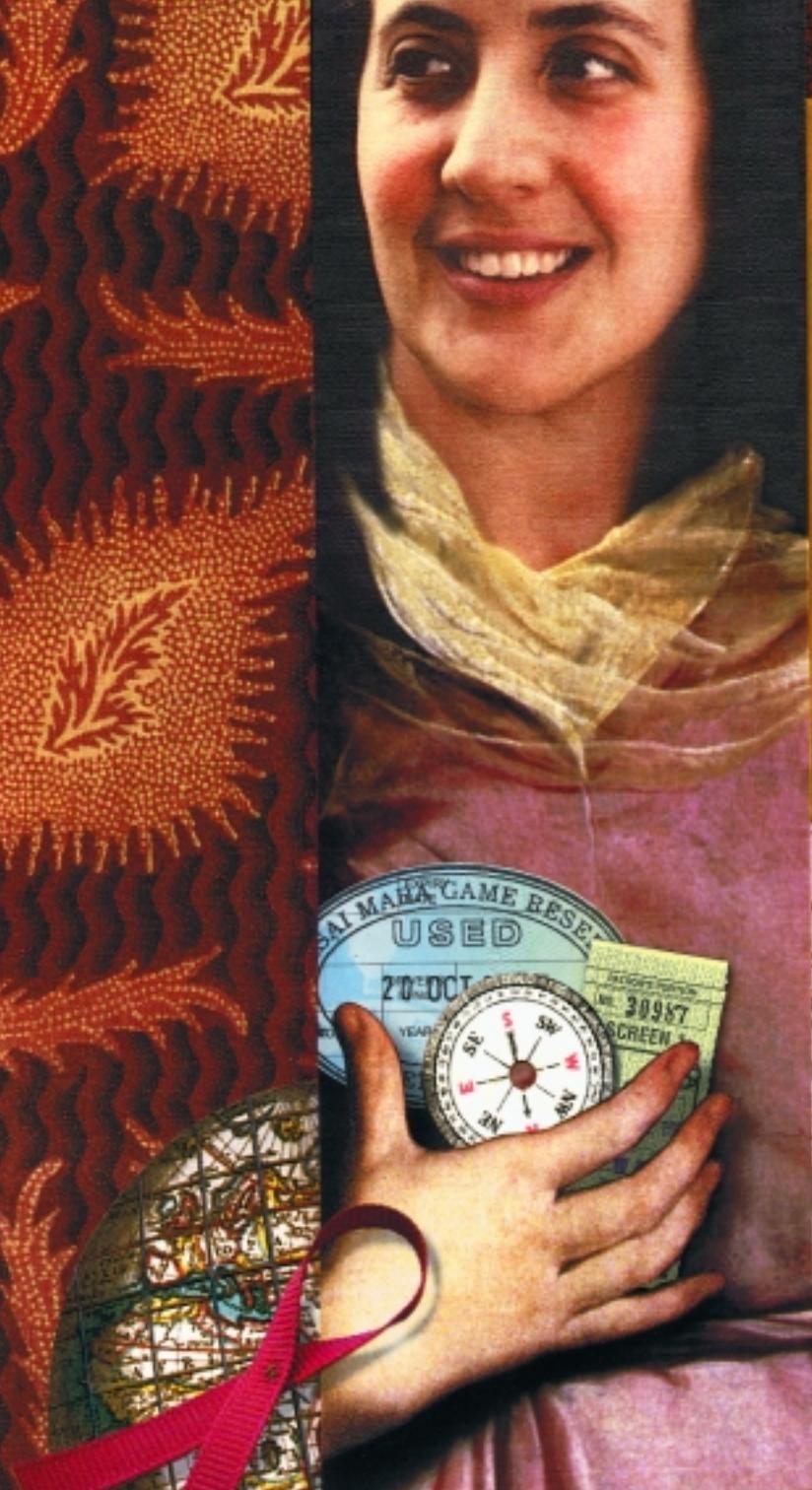
BACHRACH

Dorothy M. Horstmann made significant contributions to science, education and public health, especially to polio and rubella research. In 1942, she came to Yale to work with John Rodman Paul, and the following year she joined the Yale poliomyelitis unit. In 1961, she became the first female full professor at the medical school. Among her many achievements, she demonstrated that the polio virus reached the nervous system by way of the blood, a discovery that made polio vaccines possible. Later, Horstmann evaluated the oral vaccine program in Russia and studied the effectiveness of a rubella vaccine. She was elected to the National Academy of Sciences and also served as president of the Infectious Diseases Society of America.



Dorothy Horstmann

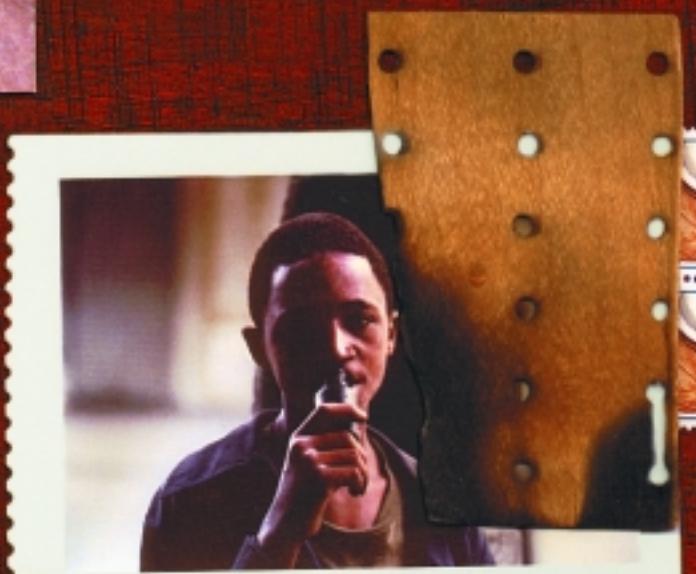
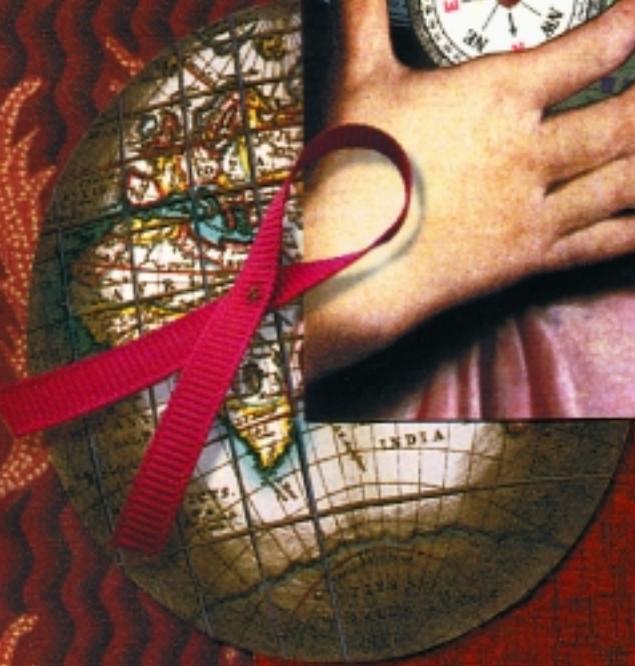
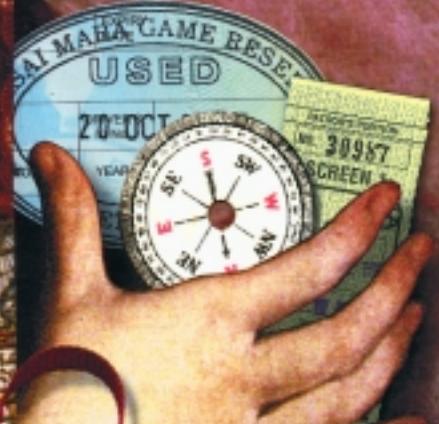
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Letter from Nairobi

Moving beyond fear

Collage
by Janis Melone
Photographs
by Tara Murphy

By Karen Schmidt,
M.P.H. '00

In Kenya's lively and cosmopolitan capital, where HIV has made alarming inroads, there's a desperate need for good prevention strategies. The right message, it seems, is one that encourages self-respect.

November 2001

It's a hot Wednesday in February, the evening rush in Nairobi is just starting, traffic is heavy and I have just swung my Subaru into a jammed-up roundabout in the Westlands section of the Kenyan capital. Most busy intersections in Nairobi feature a roundabout (we would call it a traffic circle or rotary in the United States), instead of traffic lights or stop signs. I've more or less gotten the hang of driving in Kenya—keep left, watch out for matatus (the speed demon minibuses that serve as the main form of public transport) and remember that the cars in the roundabout have the right of way. Since it's rush hour, there's even a cop directing traffic at this particular roundabout. I slip happily into what looks to be an open lane, but turns out to be the wrong lane for where I want to go. The officer notices my opportunism, looks at me in disbelief and waves me over. I put on my most respectful face and say, "I'm sorry, I'm new in town and still learning about roundabouts." I hold that this might have worked back home,

but the word “learning” only makes him more suspicious, so he rounds the car to speak to my colleague in the passenger seat; he must figure that, as a male, my co-worker is certainly in charge.

“Is this driver under instruction?” the cop asks.

“No, she’s just new in town,” says my colleague, C.Y. Gopinath, better known as Gopi.

“Where are you from?” asks the cop. I lean over and say, “U.S.,” with a big American smile. The cop looks even more suspicious when Gopi says, “I’m from India.”

The officer continues addressing Gopi. “Is she your wife?”

“No, we work together.”

“Where?”

“*path*.”

“What?”

“*p-a-t-h*. Program for Appropriate Technology in Health. It’s an *ngo* [nongovernmental organization]. We work on *aids* prevention.”

“You give medicine to people?”

“No, we help keep people from getting infected.”

I decide to pipe up. “We give them information they need to protect themselves,” I say. In fact, a basic tenet of behavior change communication (*bcc*) is that information is often not enough to change a person’s behavior, but I am trying to avoid a tragic citation, not teach a lesson on *bcc* theory.

The officer mulls the idea of prevention for a few seconds before returning to known territory. “What are the symptoms?”

“*aids* doesn’t have any symptoms on its own,” Gopi explains. “It’s when your body’s *askari* goes to sleep.”

We launch into an analogy that has proved very useful here. An *askari* is a watchman or security guard (very common in this high-crime city). When your *askari* is asleep, any thug can get into your house. *hiv* eventually puts your body’s *askari* to sleep, so any disease can get in unchallenged. One could quibble about the analogy’s accuracy from a scientific point of view, but it helps meet one of my project’s key communications objectives: increasing the perceived distance between *hiv* and *aids*. The idea is that if people believe being infected with *hiv* is the same as having *aids* and dying, they are less likely to be interested in being tested and more likely to stigmatize those with the virus. Understanding the difference also makes the point that you can’t tell if a person has *hiv* by his or her appearance.

CLOCKWISE FROM TOP LEFT
Traffic flows heavily toward a roundabout in the Westlands section of Nairobi, where a traffic stop yielded a discussion of *AIDS* and an analogy: “It’s when your body’s *askari* goes to sleep.” A real *askari*, or watchman (top right), checks author Karen Schmidt’s

identity at the entrance to her apartment complex in the city’s Lavington section. In the central business district, a man stands by one of Nairobi’s many *matutus*, waiting to drum up business while a child peers from a window of one of the brightly colored buses.

SCARE TACTICS A FAILURE

In 1999 Kenya’s president, Daniel arap Moi, declared *aids* a national disaster, and prevention and control efforts have been stepped up since then. Since August 2000, when I came to Kenya a few months after finishing my *m.p.h.* at Yale, I have been working on the communications component of *impact* (Implementing *aids* Prevention and Care), a global project funded by the United States Agency for International Development (*usaid*) and managed by Family Health International, a nonprofit based in North Carolina. My agency, *path*, is a Seattle-based nonprofit that employs about 365 people worldwide, with a mission to improve health, especially that of women and children. *path*’s Kenya site, with about 25 employees and still growing, specializes in using innovative communications methods to change behavior, focusing especially on adolescent reproductive health, prevention of cervical cancer, eradication of female genital cutting and *hiv* prevention. In Kenya, *path* implements the communication and training components of *impact*.

Though I function as a program officer for *path*, I’m not technically a *path* employee. I’m seconded to *path* Kenya through a somewhat complicated mechanism called the University of Michigan Population Fellows program. Funded by *usaid*, the program places early-career public health professionals in *usaid* missions and contracting agencies for two-year assignments; the goal is to provide technical assistance to the agency and professional experience for the fellow. My paycheck comes from the University of Michigan, and the funding comes from *usaid*, but what’s most important for me is the opportunity to work in the field just out of graduate school. At Yale I had gained a strong academic background in *epi*’s International Health Division and learned a great deal about the research, community and policy context of the pandemic while working as community director at the Center for Interdisciplinary Research on *aids*, based in the School of Public Health. But with no experience living and working in a developing country, the fellowship was just the jump-start my career needed. One thing that is clear in Kenya—and in most of sub-Saharan Africa—is that nearly two decades of awareness raising and scare tactics have not done enough to curb the epidemic. People have heard of *aids*. They fear it. Many know *aids* is caused by a virus spread through sexual contact and have some idea of how to prevent transmission. But as my



encounter with the tragic cop demonstrated, real understanding is generally poor. Myths and conspiracy theories abound—I recently heard that *aids* stands for “American Invention to Discourage Sex”—and when we ask people at outreach or training sessions to write down their questions about *hiv* and *aids*, someone always asks, “Where did *aids* come from?”

People do have a strong sense that the *aids* epidemic is a powerful force in the country and on the continent. Kenya has been measuring *hiv* prevalence since 1985, mostly through sentinel surveillance at prenatal clinics, and the statistics show that an estimated 14 percent of Kenyans aged 15 to 49 are infected with *hiv*. Though that rate is lower than those in some southern African countries, where adult prevalence may top 30 percent, it still suggests that in Kenya more than 2 million of the country’s 30 million people are living with *hiv* and *aids*. Hundreds of homeless children roam the streets of Nairobi, many of them *aids* orphans. Kenya’s daily newspapers carry pages of obituaries each day, most with photos. Usually readers are left to wonder whether the young person pictured died of *aids*, but in July, for the first time, one family had the courage to reveal their loved one’s cause of death: the color picture was flanked by two small red ribbons, the symbol of *aids* awareness.

A LANDSCAPE OF BEAUTY AND DANGER

Kenya is one African country most Americans have heard of, thanks to the film *Out of Africa* and the romantic idea of the big-game safari. Kenya does have spectacular natural beauty. Parts of the country fit the stereotype of the African desert, especially in the sparsely populated north, toward the Sudanese and Ethiopian borders, and the Taru Desert of the southeast. Shaba Game Reserve, in the semi-arid lowlands north of Mount Kenya, was the location for the third installment of *Survivor*, the popular *cbs* series. But Kenya also has lush green highlands in its Central Province, gently rolling hills and forests in the west toward Lake Victoria and Uganda, and the steamy Indian Ocean coast, with its distinct Islamic Swahili culture. The Great Rift Valley is home to the earliest human ancestors. Snowcapped Mount Kenya, at 17,000 feet, is the second-highest mountain in Africa, and Kilimanjaro, the highest peak on the continent, is just over the border in Tanzania. Numerous game parks preserve Kenya’s rich wildlife; on my first trip to Masai Mara Game Reserve a year ago last October, I saw elephants, lions, rhino, buffalo, hippos, wildebeest, giraffes, zebra and more, as well as a startling variety of

CLOCKWISE FROM TOP LEFT
Nairobi is a vibrant capital of 3 million people but its skyline, seen over the trees of Uhuru Park, suggests a smaller city. A large segment of the population lives without sanitation or running water in slums such as Kibera (top right),

which has a population estimated at 1 million. Thirty minutes from the downtown is Nairobi National Park, where impala roam in great numbers. Women sell maize and other produce in one of the city’s many markets.

antelopes, primates and birds. Watching a cheetah patiently stalking an impala, or a mama lion playing with her cubs, is unbelievably magical.

Nairobi is a busy, vibrant, cosmopolitan capital of about 3 million people, where virtually any goods and services are available to those who can afford them. Although it sits just south of the equator, Nairobi’s 5,500-foot altitude keeps the climate delightful most of the year, with the chilliest weather in July and August. Despite the country’s natural resources, Kenya’s economy is in trouble; the *gdp* actually shrank in 2000. The country recently tied with Cameroon, Bolivia and Azerbaijan as the fourth-worst in the world for corruption, according to a survey by Transparency International, a global coalition devoted to curbing corruption. Unemployment is common, crime is rampant and government services are generally poor: roads are in bad shape, many police don’t have vehicles and garbage collection is sporadic or nonexistent. A large proportion of Nairobi’s population lives in slums without running water or sanitation. For most of 2000, the power company was rationing electricity because a drought had reduced the country’s hydroelectric output; in some places, power was cut for 12 hours a day, and water was in short supply. The political climate is uncertain because President Moi, who came to power in 1978, is constitutionally barred from running again in the 2002 elections; some wonder if he will try to run anyway, but in any case the next year is sure to be unsettled.

For people in Nairobi, the terrorist attacks of September 11 brought back the horrors of August 1998, when the U.S. Embassy here was bombed. A total of 213 people, most of them Kenyan, died in the attack, believed to be the work of Osama bin Laden’s Al Qaeda organization. Thousands were injured. Many businesses moved out of the congested city center after the bombing, but since security is already a priority here because of crime, the effect on daily life post-September 11 has been minimal.

In this context, convincing individuals to worry about a virus that may kill them in a decade or so can be a challenge. At *path*, we’re trying to devise new ways to improve the effectiveness of peer education, the centerpiece of the *impact* project, with the ultimate goal of persuading people to protect themselves by using condoms, reduce the number of sexual partners and learn their *hiv* serostatus through voluntary counseling and testing. Given that the vast majority of infections in Kenya occur through heterosexual sex, our premise is that *aids* is not the problem, but the consequence: the problem is relationships. That includes relationships between a husband and wife, a young man and woman, a commercial sex worker and



Wildbeest and satellite TV: an expat's African existence

Maybe I'm just used to it, but some days, life in Nairobi seems indistinguishable from life in New Haven. I get up, make coffee, drive to work listening to silly contests and chatter on the radio ("KISS 100, Nairobi's Fresh Hits"), spend the day pecking at a keyboard, attending meetings and juggling phone calls, and then head home. I might stop at the gym or the supermarket, or call a friend on my mobile phone on the way, and maybe arrange to meet for pizza or sushi or Indian food. I've found it relatively easy to meet other ex-pats to hang out with; we might go to the mall to eat at the food court and see a movie. Back home at my apartment complex, I might catch something on DSTV (digital satellite television) or go for a short walk if I've managed to get home in time—the sun sets around 6:30, and walking after dark is dangerous. If it's too late, I can walk around the apartment complex, a compound of seven four-story buildings. It's safe behind the 10-foot wall, topped with an electric fence, with five *askaris* on duty around the clock.

Weekends offer a chance to head out of the capital city's bustle and smog. Just outside of town, beyond the suburb of Karen (named for Karen Blixen, who wrote *Out of Africa* under the pen name Isak Dinesen) are the Ngong Hills. Shaped like the knuckles of a fist, legend holds that the hills were formed when a giant tripped over Mount Kilimanjaro and rested his fist to steady himself. A walk along the spine of the hills offers a view of Nairobi on one side and a spectacular drop-off to the Great Rift Valley on the other. Venturing further away from Nairobi, there are game parks, campsites, eco-lodges, mountains to climb, lakes and the Indian Ocean.

Beyond Kenya, the two other official East African countries, Uganda and Tanzania, offer their own charms. In Uganda last March, after a weeklong workshop in its pleasant, quiet capital, Kampala,

I spent an insanely exhilarating day whitewater rafting on the Nile just below the source. While villagers on the banks watched in amazement, about 20 crazy tourists navigated class 4 and 5 rapids, even going over a four-meter waterfall backwards (on purpose, according to our very relaxed guide). In April, I visited Zanzibar, the archipelago that forms, with the mainland of Tanganyika, the United Republic of Tanzania. Stonetown, on the main island of Unguja, is a maze of narrow, winding streets, some so small you can reach out and touch buildings on either side. The culture is very Swahili and very Muslim; the Kiswahili language has its roots in Zanzibar, and Zanzibaris believe they speak its purest form. (In Kenya, most people speak a more casual version of Kiswahili in addition to their native language and at least some English.) Most Zanzibari women wear a *bui-bui* (black robe and head scarf). Wooden *dhows* in the port are still very much in use.

Wherever I go, and whatever exotic experiences I enjoy, I'm acutely aware that my privileged life here bears little relation to the lives of most Kenyans. Nairobi has a large expatriate community, working in government, business or the huge development sector. Most of us live far better here than we ever could at home, and our resources insulate us from many discomforts. When I arrived in August 2000, the city was gripped by severe power rationing and water shortages; I found an apartment complex with a backup generator and a well. I've become frighteningly accustomed to having someone else wash my clothes, clean my house and carry my groceries to my car. Most days do feel ordinary—except when I'm trying to make a phone call across town and it won't go through, or I have to stop on the way home to let a cow or goat cross the road or I decide to spend a Sunday at the Nairobi Game Park on the edge of town, looking at giraffes or warthogs or lions. Then I remember—I live in Africa. For real.

KAREN SCHMIDT

CLOCKWISE FROM TOP LEFT Actors perform during a recording session for *Kati Yetu* ("Between Us"), a national weekly radio program that carries AIDS prevention messages. Peer educators for **IMPACT** demonstrate how a condom is used in a section of

Mombasa, Kenya's second-largest city. Artist Bella Kilonzo with his poster for the second comic book in the *Nuru* series. A schoolboy in Kakamega in Western Kenya works on a mural outside Kakamega Primary School.

her client, a young girl and a "Sugar Daddy." A key goal is reducing the despair and fatalism surrounding *hiv* and replacing it with messages of optimism, hope and greater self-respect, as a prerequisite for greater acceptance and involvement with lifesaving messages about *hiv* and *aids*.

DRAMA ON THE AIRWAVES

The theme of *path's* communication strategy for *impact* is "Question Your Relationships." In every activity, people are encouraged to ask questions, not necessarily to receive the answers from an all-knowing teacher, but to begin thinking in depth about the epidemic, their own risk of *hiv*, and how the nature and quality of their relationships affect that risk. Rather than imparting information from the top down, we're training peer educators to facilitate intense dialogue and debate with a relatively small number of people. As the people in those groups raise issues and concerns, and even change their behavior, we'll magnify the issues and changes on a national weekly radio program we launched in May. The program, called *Kati Yetu* ("Between Us" in the Kiswahili language), includes a soap opera and a magazine with interviews, panel discussions, music and news. Listening groups have been formed to help spark and deepen debate on issues raised in the program; feedback from those groups, and the peer education groups, will keep the program responsive to community concerns. We depend on *impact's* large network of implementing partners to help carry out these activities; the partners, all funded by Family Health International, range from local clinics and *ngos* to the Kenya Girl Guides Association and the University of Nairobi and conduct activities such as upgrading health centers and providing voluntary counseling and testing, in addition to peer education and listening groups in workplaces and in the community.

path is also producing a comic book for youth, and did a series of murals in schools. For the latter, students developed the content through discussions and role play, then painted the murals with supervision from professional artists and wrote essays based on the topics depicted in the mural. These intense activities are more difficult than producing a poster that says "AIDS Kills." But we know that fear doesn't reliably lead to prevention, and despite the probable wider introduction of anti-retroviral drugs in Kenya, prevention remains essential.

The challenges to effective prevention are considerable. As in so many places, people are uncomfortable talking about sex and leery of talking to adolescents about sexuality. Years of

continued on page 48



LESSONS FROM ANTHRAX

The deaths of five people exposed to anthrax last fall put bioterrorism squarely on the map.

**Where does the road lead from here?
*A Yale Medicine roundtable.***

THE DISCUSSANTS

FRANK J. BIA, M.D.

professor of medicine (infectious disease) and laboratory medicine; co-director of the Yale International Health Program

JONATHAN B. BORAK, M.D.

associate clinical professor of medicine and epidemiology, board-certified toxicologist, member of the National Research Council's committee on chemical warfare agents

RAVI V. DURVASULA, M.D.

assistant clinical professor in the division of epidemiology of microbial diseases and medical director of Yale University Health Services; Durvasula has worked on projects aimed at developing pathogen countermeasures for use in bioterrorist attacks

At the 2001 annual meeting of the American Association for the Advancement of Science last February in San Francisco, an audience member asked a panel of experts on bioterrorism why the world had yet to see a major biological attack. After a moment's pause, a response came from Stephen Morse, PH.D., director of the Center for Public Health Preparedness at Columbia University. "Nobody really knows the answer to that," he said. "I suspect there have been a number of barriers, some cultural, some technical, to pulling this off. Clearly, there have been a number of groups as well as countries that have been interested. It is only a matter of time before the motivation and the knowledge of those people who wish to use bio will reach the point where you will see a real attack happen. I think, unfortunately, it is probably not that far in the future."

September 11 dispelled any doubts about barriers to perpetrating a major terror attack, and the ensuing rash of anthrax exposures made the notion of biological warfare real to Americans. The use of the mail to deliver anthrax, however, was a scenario no one on the panel of soldiers, scientists and scholars had envisioned. We wondered what Yale's experts in the field might be doing to try to anticipate the unanticipated, and in early December, Associate Editor John Curtis asked faculty and alumni in medicine, public health and microbiology to comment on the anthrax scare and bioterrorism more generally. On the following pages are highlights of their responses.

ROBERT HEIMER, PH.D. '88

principal investigator of the Yale Emerging Infections Program, associate professor of epidemiology and public health and of pharmacology

STEPHEN C. JOSEPH, M.D. '63, M.P.H.

former commissioner of health for New York City, former assistant secretary of defense for health affairs and a founding principal in the health consulting firm Black Dog Associates in Santa Fe, N.M.

RICHARD M. SATAVA, M.D.

professor of surgery, former program manager of the Advanced Biomedical Technologies Program of Defense Advanced Research Projects Agency

ANDRE N. SOFAIR, M.D., M.P.H. '97, HS '90

assistant professor of medicine; one of Sofair's research interests is the development of surveillance systems to assist in the clinical recognition of unexplained infectious diseases

Five people have died and 13 others have become infected with anthrax in its inhalation or cutaneous form as of November 24. Given these cases, how serious is the threat of biological terrorism?

DURVASULA

The threat of bioterrorism should be considered very real. We now know that a bioterrorist attack can be launched successfully in the U.S., that high-grade, highly infectious agents can be readily released in our country, that perpetrators of these acts may go undetected, that the health care system is entirely unprepared for such attacks, and that otherwise innocuous routes such as the mail may be used.

BORAK

The hoof-and-mouth infection that wiped out much of the beef herd in England in 2000 could have been an example of bioterrorism and could be readily reproduced in this country. There is an incredible ease about delivering enteric pathogens to the food sources in our very open society. Think of one person—a truck driver for a supermarket chain who sprays vegetables prior to delivery.

HEIMER

Although bioterrorism is a threat because its sources and the potential for more terrorist dissemination are unknown, the health of the American public is far more threatened by infectious agents whose disease burden could be reduced by concerted public health action. While we need to solve the criminal issue of anthrax terrorism, public health money could be more wisely spent combating the spread of preventable diseases.

What other pathogens might pose a threat from bioterrorists? Smallpox? Tularemia? Q fever? Ebola? Plague?

DURVASULA

Potential agents include bacteria such as the anthrax bacillus or plague bacillus, viruses such as smallpox or agents of hemorrhagic fever, or even toxins such as staphylococcal toxin or botulinum. The greatest threat in terms of mass lethality is posed by those agents that can be aerosolized and for which treatments are limited and natural immunity is low. Therefore, in addition to anthrax, smallpox virus, plague bacillus and *Francisella tularensis* (the agent of tularemia) are considered potential agents.

JOSEPH

Perhaps an even greater problem is modified organisms, from strains of smallpox which might be resistant to current vaccines, to the chimera organisms we know the Soviets were working on. Chimera organisms could be developed to give a one-two punch where a second illness would break out after the first illness.

What can we learn from the anthrax scare this fall?

JOSEPH

We were very fortunate in two ways. It was a noncontagious agent and the mechanism of dispersion used was relatively inefficient and very small-scale.

In general, our disaster management programs in the states involve three sectors: law enforcement/military, disaster management/environmental protection, and public health/clinical medicine. Traditionally, the public health and clinical part of that triad has been sort of a dragging dog. It is the law enforcement—and in some cases the military—that runs the operation. Except for industrial or chemical events, the health problems have been largely surgical triage and response. In the biological and chemical warfare world we are now in, that changes. The subtleties, complexities and degrees of uncertainty are so different that public health and clinical medicine need to take a much more expanded and important role.

HEIMER

We need to broaden existing ER and primary-care surveillance. Quick response means quick detection of suspect cases, rapid diagnosis, proper identification of and prophylaxis for those exposed. Immediate attempts to trace the source of infection and, in the case of agents that can be transmitted easily from person to person, the contacts of the index case must become routine parts of such surveillance schemes.

What needs to be done to prepare our public health infrastructure to deal with biological warfare?

JOSEPH

The infrastructure at the municipal and county levels is underfunded. It's weak. It is not well coordinated with the clinical sector or the law enforcement sector. It often doesn't do a good job with the media. In all sorts of ways we need to beef up everything, from computerized information systems that link horizontally as well as vertically, to increased laboratory resources, to tighter relationships between the clinical and public health sides.

BORAK

I have been trying to push the American College of Occupational and Environmental Medicine to develop models so that corporations can use their existing facilities as adjuncts to the public health system. Most large corporations already deal with trying to get most of their employees to take flu shots. Let's assume that it was necessary to vaccinate the entire population of a city. There is no way the city's department of public health is going to do it. They don't have the capacity. You could find the 50 or 100 largest employers and simply deputize them. You could ask corporate medical directors, "Can you develop a system so that any one of your facilities would be able to provide, within 48 hours, vaccinations for every employee and his or her immediate family?" It is a system that already exists. It just doesn't know it exists.

What can this medical school do to better educate students and physicians to deal with biological terrorism?

SOFAIR

We need to think about which diseases we teach the students about. We need to teach students how to recognize something unusual, even if it is presenting in a common syndrome. Many of the agents that may be used in a bioterrorist attack may present as a pneumonia, or an encephalitis, and may be indistinguishable from more common etiologies without a high index of suspicion. And we need to teach our medical students how to take a good exposure history.

BIA

Our curriculum in medical microbiology is readily adaptable to dealing with the pathogenic features of potential bioterrorist agents. Much more difficult are the terrorism pieces. What conditions breed terrorism? How do lack of adequate health care, poverty and instability foster terrorism? This is not just a “wet bench” problem. It involves the social sciences—the very disciplines that physicians tend to avoid as “soft.”

Since the first case of anthrax was diagnosed this fall in Florida, information released to the public has been at times contradictory and at times inaccurate and incomplete. How can the federal government better coordinate its communications regarding biological threats?

JOSEPH

Public health people have to learn how to get out in front and make sure that political figures and the media are passing along good, consistent and useful information that helps the medical and public health process along.

HEIMER

Speaking with a single voice is not necessarily speaking the truth. A free society needs multiple sources of information and an appreciation that contradictory messages are a necessary part of a free society’s emerging response to the unknown. Only totalitarian states can choose a single path and adhere to it regardless of what new information becomes available.

Are there ways of safeguarding potential conduits for bioterrorism? In the case of anthrax, this might mean irradiating the mail. What other channels are vulnerable and how might they be protected?

HEIMER

It’s hard to comprehend all the possibilities. Life is not without risks, and if we considered all the possible risks and tried to prevent them, we would still be living in caves. The proper question is, “How should we respond when a new threat emerges?”

SATAVA

The solution to bioterrorism is not technology. I am not convinced that a huge investment in many of these preventive measures—which can drain our economy—is capable of preventing such acts from occurring. The solution is to eliminate the root cause, or perceived root cause, which may be impossible. Temporizing solutions, such as tearing up the Al Qaeda network, are essential in the near term, but better long-term solutions on a multinational level are also required.

Is the hoarding of antibiotics a public health threat in and of itself? How can people protect themselves without resorting to prophylactic use of antibiotics?

DURVASULA

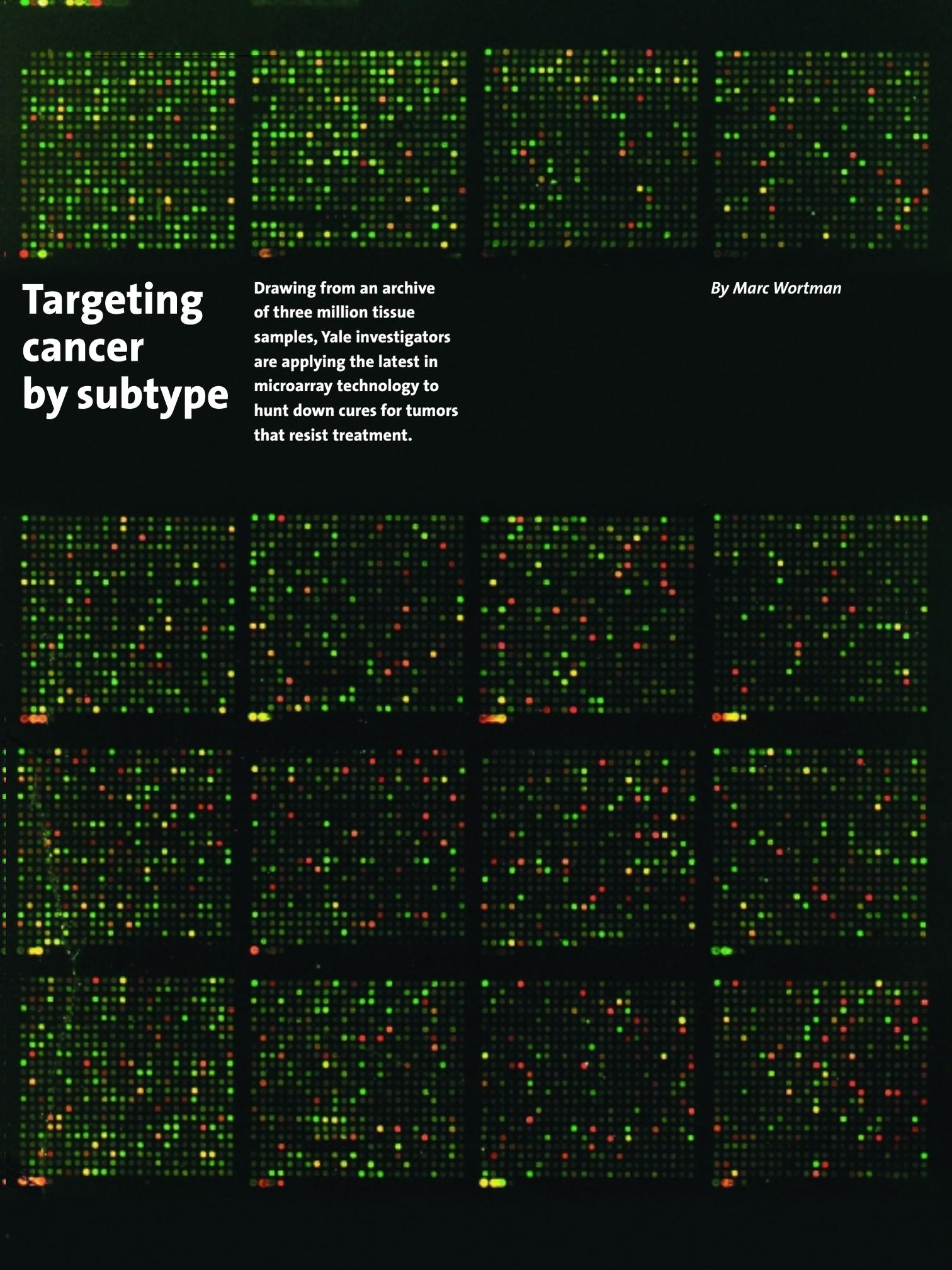
The hoarding of Cipro is a public health nightmare, since it may lead to a shortage. There are numerous reports that people are taking the medications erratically, because of unpleasant side effects. This is a recipe for disaster in terms of emergence of antibiotic resistance. With the current anthrax scare and potential future bioterrorist threats, society may easily slide backward in the effort to use antibiotics wisely, creating a far greater epidemic of antibiotic resistance.

HEIMER

Compared to the overprescribing of antibiotics for all forms of viral disease, the current overuse of Cipro is a blip on the radar. For health threats, it makes sense that health officials at the municipal and state levels, with the backing of experts at the **cdc**, be given the forum they need to articulate who, if anyone, in their community needs medical prophylaxis. Individuals in this society are free to accept or disregard this advice, but it’s important that the advice offered is sound medically and inclusive of all those at risk.

SATAVA

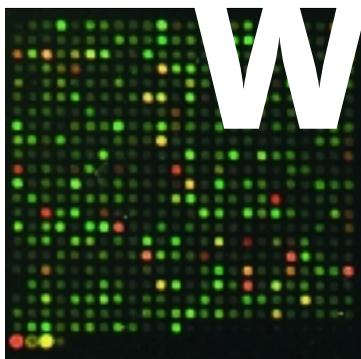
The bioterrorist threat cannot be solved with stockpiling of antibiotics or vaccination against all possible agents. I don’t believe that anyone can protect themselves against bioterrorism, just as we cannot protect against nuclear holocaust. Bioterrorism has become a fact of life, and we as a nation must adjust, accept that we might possibly be subject to a horrific act and go on with our lives. In the meantime, we should develop only those technologies and response systems which have a high likelihood of mitigating specific areas of risk. **VM**



Targeting cancer by subtype

Drawing from an archive of three million tissue samples, Yale investigators are applying the latest in microarray technology to hunt down cures for tumors that resist treatment.

By Marc Wortman



When a pathologist looks at the biopsy of a suspicious lump, she checks for the telltale signs of cancer—the clumping of cells and distortion in their normal architecture—that reveal a malignancy. From there, she may test for biological markers that categorize the cancer, hoping to

guide oncologists as precisely as possible in making treatment choices for the patient. That's the hope, anyway. All too often, though, one cancer looks and tests very much like another. Yet chemotherapy will melt away one patient's tumor, while having no effect on another, seemingly identical cancer. At that point, it may be too late to pursue other therapies, including experimental treatments that might have helped if used earlier on.

Genetic oncologists are beginning to understand why cancers that look the same react so differently to treatment. A range of new and related molecular technologies has begun to reveal a surprising fact about cancer: melanoma, lymphoma and virtually all other major cancer groupings have genetic subtypes, some of which resist treatment or may respond better to different therapies. Although the symptoms and the cells appear the same, they are effectively different diseases.

The effort to define these subtypes begins with a map of the genome of the cancer cell. Once armed with that knowledge, pathologists will know whether one therapy or another will be more likely to work for the specific cancer subtype. It also provides tools for seeking out new and better treatments.

That is why Vincent T. DeVita Jr., *m.d., hs '66*, director of the Yale Cancer Center, and colleagues decided in February 2000 to launch the Yale Tissue Microarray Facility. Together with the Keck Biotechnology *dna* Microarray Resource, which was expanded in 1999 with funds from the National Cancer Institute (*nci*), it provides scientists at Yale and other research centers around the world with a powerful set of tools for experiments to get at the genetic underpinnings of cancer. "I don't know of a single cancer that doesn't have an identifiable genetic abnormality," says DeVita, a former *nci* director under Presidents Carter and Reagan and author of the leading oncology textbook. Once known, that abnormality becomes

OPPOSITE A portion of a glass slide DNA microarray shows the differences in gene expression between two human cancer cell lines. A single array can hold segments of more than 18,000 genes. Red spots are genes expressed only in one cell line and green spots are

genes expressed only in the other. Yellow spots represent genes expressed equally in both lines. Similar comparisons can be made between tumor cells and normal tissue and in malignant cells at various stages of their development.

a potential marker for early detection and a precise target at which to shoot chemical compounds for a possible cure.

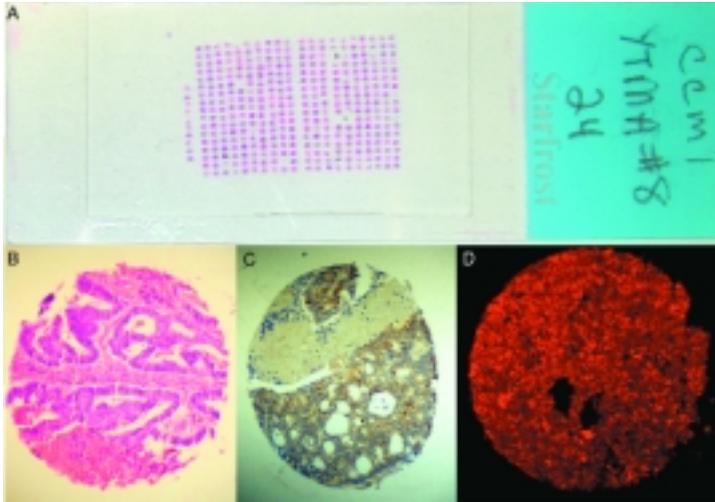
The Tissue Microarray Facility and the *dna* Microarray Resource are part of a series of initiatives at the Cancer Center and elsewhere at Yale to apply the emerging technology of microarrays to the study of basic biology, cancer and other diseases. Most importantly, microarrays hold the potential for rapid advances in the design of new treatments. "You can address real and important questions with arrays," says DeVita. "They're going to be the tools for the future. I don't have a crystal ball, but if I were a betting man, I'd bet that new treatments will happen faster than anyone expected previously because of them." In fact DeVita has made some big bets at Yale that those technologies are key to coming up with better ways to find and treat cancer.

CHIPPING AWAY AT CANCER

Microarrays, sometimes referred to as biochips, are created by positioning minute amounts of biological material, such as tiny slices of tissue or portions of genes or proteins, on a glass microscope slide or a computer chip. Robots drip nanoliter quantities through tiny tubes—in some instances spraying spots out like an inkjet printer and in others placing tiny droplets like a quill pen—at precisely known positions to create a matrix of spots on the chip's or slide's surface.

There are several ways of capturing data from microarrays, which use either electrical current or biochemical reactions to measure gene and protein expression or the properties of tissue. The arrayed material—chemically tagged with a fluorescent compound—can be treated with chemicals, complementary *dna*, messenger *rna* or other proteins, with which it interacts. The fluorescent tags light up during the reactions, and laser scanners pick out the glowing spots. Computers read and display the results quantitatively or graphically. The green, red, and yellow colors of gene expression arrays, indicating genes that are active in a cell, have become something of a signature image for microarray technology.

Where previous methods allowed one gene, protein or tissue sample to be studied at a time, a single microarray can be used to look simultaneously at virtually every gene in a cell or at tissue samples from hundreds of patients. A single glass slide *dna* array can hold segments of more than 18,000 genes, and a few slides provide sufficient capacity to study every known gene in the human genome or all the genes in model organisms such as yeast or certain bacteria.



DAVID RIMM (2)

Tissue microarrays provide a means of analyzing hundreds of tumor samples simultaneously while conserving scarce sample material. Unlike gene chips, in which each spot represents a sample of cloned *cDNA*, tissue microarrays contain tiny plugs of tissue extracted from storage in paraffin blocks. The composite image (top) shows an array of 340 colon-tissue samples and closeups of individual spots stained using three different methods. The breast-tissue blocks for a single microarray (above) nearly fill a laboratory.

Experiments result in the quick generation of massive amounts of information—a mountain of data whose interpretation requires a combination of biology and computing skills that is currently in very short supply. Though there are many other bottlenecks in the ongoing development of technologies, microarrays already allow investigators to make advances far beyond what was possible with previous study tools. “An array gives you an all-inclusive opportunity to look at genes or tissue and to get a complete and much more accurate answer. There are hundreds of questions that could be addressed this way,” DeVita says. At least a dozen laboratories at Yale in departments including Genetics; Molecular, Cellular and Developmental Biology; and Pathology and the Section of Immunobiology are now using biochips to unlock the mechanisms of diseases, especially cancer.

Yale is home to one of 24 *cDNA* microarray centers set up in 1999 at cancer centers around the country with *nci* funds. The Howard Hughes Medical Institute supplemented those funds at Yale’s Keck Foundation Biotechnology Resource Laboratory. Archibald S. Perkins, *m.d., ph.d.*, associate professor of pathology and of molecular, cellular and developmental biology, co-directs the *cDNA* Microarray Resource, which produces biochips for laboratories at Yale and around the world. Perkins uses microarrays in his own research to study how leukemia changes cells at the molecular level, in hopes of coming up with new targets for drug therapies. Microarrays permit him to study all the genes that are turned on in leukemia cells at various stages of their development. Before the advent of microarrays, that was impossible. “It’s really a fantastic achievement,” he says.

According to Co-Director Janet Hager, *ph.d.*, the capacity of the arrays has doubled in the last year, to a current maximum of 18,432 spots. “We now offer five different arrays for human and mouse,” said Hager, “some representing as many as 16,000 unique genes in the form of either *cDNA* or oligonucleotides.”

Much of the data produced remains undeciphered, and some laboratories specialize in studying raw data that gets posted on public websites. According to Perkins, “There’s almost a community effort to make sense of the results.” A major initiative is under way to create the Yale Microarray Database through the collaborative efforts of a group of investigators and the Yale Center for Medical Informatics.

Though it is still an emerging technology, the data flood has begun to resolve a number of long-standing puzzles, such as why certain cancers that appear to be identical under the

pathologist's microscope respond so differently to treatment. Small genetic differences are the key. When coupled with all the gene sequence data from the Human Genome Project, microarrays are giving scientists tools for understanding the genetic changes that take place when a normal cell becomes cancerous. Knowing the genetic defects specific to a cancer offers a potential diagnostic tool and gives pharmacologists a starting point for drug discovery. "We can now aim for a unique cancer target," says DeVita, adding that such designer drugs hold great promise against previously untreatable cancers. One successful example is Gleevec, a pharmaceutical designed to cure certain forms of previously untreatable leukemia and a rare stomach cancer. "Gleevec is the most effective targeted treatment ever for leukemia," he says. "It puts us in the era of specifically designed therapies. We're going to see lots of them from now on."

SCORING A DIAGNOSIS

In 1999, *nci* scientists developed the tools to make tissue microarrays for two reasons: to stretch out limited supplies of tissue and to standardize conditions for studying and comparing multiple samples. A single array can hold as many as 800 half-millimeter cross sections of tissue and can complement other types of large-scale studies in a variety of ways. Unlike tissue arrays, gene chips cannot be used with large patient populations because of their complexity and the huge amount of data that even a single *dna* array generates. Laboratory results still require validation in larger, statistically verifiable studies, especially before expensive and complex clinical studies can begin. Studies of hundreds of patients can be done with a single tissue microarray—with minimal tissue expended—as a way of validating what was seen in other types of pilot experiments.

Yale is exceptionally well placed to take advantage of the new technologies because of its huge collection of cancer tissue samples. Early last century, Yale pathologists began to store tumor sections from cancer patients at what was then New Haven Hospital. The standard practice at the time, as it still is in most hospitals, was to keep pathology samples around for a few years and then discard them. Yale kept many of the tissue samples on hand as a study and teaching collection, and they have contributed to what is now known as the Yale Tissue Archive.

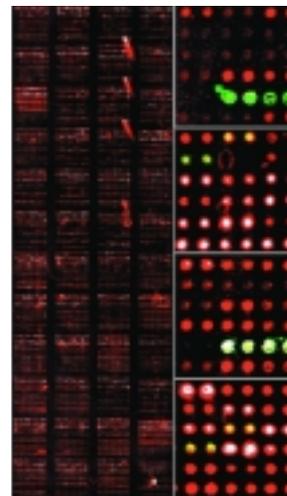
The pieces of tissue are, for the most part, plugs smaller than a thimble. They are embedded in paraffin blocks and

Powering protein chips

Protein arrays are the least developed of the emerging biochip technologies and very likely the most complex. Every gene codes for at least one and often many proteins, the macromolecules that carry out the activities necessary for life. While current estimates of the number of human genes range from 30,000 to 100,000 (with about 10,000 of them already mapped), the number of proteins encoded by those genes may number in the millions. Most cellular development and other life functions result from the myriad interactions of proteins, and most disease and other disorders result when those interactions go awry.

That is why a paper in the September 14 issue of *Science* by Michael Snyder, Ph.D., professor and chair of molecular, cellular and developmental biology, and colleagues attracted broad interest. They reported successful development of a chip that held virtually all 6,200 proteins of yeast on a single microarray. No array had ever held the complete proteome of an organism before. While the technology is still in development, many fundamental protein interactions, some shared with humans, can now be studied in a global manner, just as can the genes that code for proteins. A new company, Protometrix Inc., was founded in Guilford, Conn., based on Snyder's work with proteome chips.

Snyder's team is now attempting to create a human proteome chip. He also plans to use proteome chips in his own research at Yale's new Center of Excellence in Genomic Science, which he directs. The National Human Genome Research Institute awarded Yale a \$15 million, five-year grant this fall to search for gene and protein function (See *Chronicle*, page 7). Yale was one of only three recipients of the awards. (Two separate centers at the University of Washington at Seattle received the other grants.)



Michael Snyder and colleagues at Yale and North Carolina State University spotted nearly all the 6,200 proteins in yeast on a single, nickel-coated glass slide.

HENG ZHU

kept in labeled cabinets in the basements beneath the medical school and in the hospital. In 1935 the state of Connecticut established the Connecticut Tumor Registry, requiring all hospitals and clinics in the state to report every case of cancer, along with follow-up, treatment and survival data. It was the country's first such database. With the establishment of the Tumor Registry, pathologists began to archive patient information along with tissue at Yale.

In the early 1980s, Jon S. Morrow, *ph.d.* '74, *m.d.* '76, *hs* '77, who is now chair and the Raymond Yesner Professor of Pathology, headed a team that developed a clinical database for tracking tissue pathology and patient information. (That system, known as CoPath, is now in wide use around the world.) With support from Yale-New Haven Hospital, available records for tissue in the Yale archive were entered into the CoPath database, which today covers more than 3 million separate tissue samples taken from about 1 million patients. At Yale, one can locate virtually any form of cancerous tissue or group of related tissues, compare treatments and their effects and follow the course of the disease. "If we go looking for a specific type of cancer, it's there," says David L. Rimm, *m.d., ph.d., hs* '91, associate professor of pathology and director of the Tissue Microarray Facility. "The samples are usually thick, and we have instant 20 to 40 years of follow-up."

The combination of massive tissue archive and computerized database may also have a big impact on the future practice of medicine. Robert L. Camp, *m.d., ph.d.*, an associate research scientist in Rimm's laboratory, has developed software that can automatically "score" tissue arrays—that is, compare a cell's features to those of other cancer or normal cells. The software, called Aqua, could eventually be used to measure tissue properties to determine the likelihood of response to therapy. Recognizing its commercial potential, the Office of Cooperative Research has been working with Rimm, Camp and outside investors to build a new company to develop it into a marketable diagnostic tool.

"Aqua," says Rimm, "could replace some of the tasks currently done by a pathologist. There may ultimately be a day when pathologists run machines as opposed to making a subjective determination of a diagnosis. It's going to happen sooner rather than later."

ARRAYS FOR THE FUTURE

The various microarray tools could eventually find their way into clinical use. Some predict that the first biochips for

diagnostic purposes will be seen in hospitals within two years. Within the next decade, chips could indicate to pathologists that telltale genetic markers for early forms of cancer are present, opening the door to earlier treatment before the malignancy spreads.

All the new technologies must be developed further, however, if they are to prove more than tools for the laboratory. "You want something that is inexpensive, simple and fast," says Associate Professor of Pathology Paul M. Lizardi, *ph.d.*, who has invented several array-based technologies, including rolling circle amplification and whole genome amplification, which rapidly amplify genetic material for easier use of microarrays as diagnostic tools. Two New Haven companies, Molecular Staging Inc. and Agilix, have licensed technologies he developed at Yale for improved detection of *dna* using microarrays. Says Lizardi, "Microarray technology is too expensive today, and it has not yet been optimized for clinical use. There's a real need for microarray-based tools that are cheaper and better."

Many Yale scientists are confident that as microarray technology becomes refined it will lead to progress at an unprecedented pace. In his laboratory DeVita hopes to find genes common to different cancers that resist standard chemotherapy. "If you find one gene that triggers a family of genes associated with drug resistance," he says, "you could use the knowledge to solve a universal problem. That would be a tremendous advance."

According to DeVita, all the new tools will soon provide patients with ever-more-precise diagnoses and effective treatments for cancer. "In the not-too-distant future," he says, "cancer will be a chronic disease treated on an ongoing basis like diabetes or hypertension. This is the real payoff. It is what we've spent \$42 billion for in the war on cancer." **YM**

MARC WORTMAN is a contributing editor at *Yale Medicine*.



Michael Merson



Michael Bracken



Brian Leaderer



Hongyu Zhao

FOUR FACULTY MEMBERS IN PUBLIC HEALTH HONORED WITH ENDOWED CHAIRS

Four faculty members with appointments at the School of Public Health were recently named to endowed chairs.

Dean **Michael H. Merson, *m.d.***, was named the Anna M.R. Lauder Professor of Public Health; **Michael B. Bracken, *m.p.h.* '70, *ph.d.* '74**, and **Brian P. Leaderer, *m.p.h.* '71, *ph.d.* '75**, were each appointed Susan Dwight Bliss Professor of Public Health; and **Hongyu Zhao, *ph.d.***, was named the Ira V. Hiscock Associate Professor of Public Health and Genetics.

Merson is a noted authority on *aids* and director of Yale's Center for Interdisciplinary Research on *aids*, which was established in 1997 to support *hiv* prevention research in vulnerable and underserved populations in the United States and abroad. He focuses his own work on international aspects of *hiv* prevention and related policies. Prior to his involvement in *aids* research, Merson undertook studies of the epidemiology of diarrheal diseases, including cholera, in developing countries.

Following his medical training Merson spent three years working for the Centers for Disease Control and Prevention, and then became the chief medical epidemiologist at the Cholera Research Laboratory in Bangladesh. From 1978 until 1995 he worked for the World Health Organization (*who*) in Geneva, and from 1990 to 1995 he headed the worldwide effort to control the *aids* pandemic as the director, then executive director, of the *who's* Global Programme on *aids*.

At Yale Merson also directs the *aids* International Training and Research

Program, based in St. Petersburg, Russia, and the *aids* International Clinical, Operational, and Health Services Research Program based in Pretoria, South Africa. Both programs are supported by the National Institutes of Health's Fogarty International Center. He has been a consultant to the World Bank and to its *aids* prevention projects in such countries as India, Russia, Bangladesh, Nigeria and Madagascar. He has chaired several national panels and committees focused on the prevention of *hiv* and other diseases.

Bracken is head of the Chronic Disease Epidemiology Division in the Department of Epidemiology and Public Health. He specializes in the epidemiology of diseases of pregnant women and newborns and has been instrumental in developing therapies for acute spinal cord injuries. He combines these interests in his research and as director of the Yale Perinatal Epidemiology Unit and the National Acute Spinal Cord Injury Study. The former, which he has led since 1979, conducts research on obstetric, perinatal and neonatal disease. The latter, which Bracken has overseen since 1977, conducts randomized trials of therapies for preventing paralysis after spinal cord injury.

Bracken and his colleagues identified the first successful therapy for acute spinal trauma in 1990. His articles in this area have examined the effectiveness and timing of the drugs methylprednisolone and naloxone in treating spinal trauma and the effectiveness of surgery in combination with drug therapies in treating spinal cord injuries.

Leaderer is a noted authority on air quality whose research focuses on assessing exposures to air contaminants and the health impact of such exposures.

Following tradition, the members of the Class of 2005 posed in their newly donned white coats on the steps of the Sterling Hall of Medicine. **BELOW RIGHT** New first-year students Samantha Wood, Sandra Smith, Bradley Raphael, Daniel Gibson, Jorge Galvez, Meg Pearson and Douglas Jacobson (from left) linked arms at the White Jacket Ceremony. **BELOW LEFT** Lianne Hirano wore two leis, one made by her friend, Cheryl Teso, and the other, made with orchids, sent by her mother from Hawaii.



TERRY DAGRADI (3)

**FUND-RAISING EVENT,
NOW A FALL TRADITION,
TAKES A DIFFERENT TACK**



In a break from tradition, anatomy professor William B. Stewart, *ph.d.*, sold his trademark bow tie this year not at the Hunger and Homelessness Auction, but at a party a few days before the gavel banged down. It was one of many subtle departures from the traditional format of an event that is now in its ninth year of raising money for New Haven charities. The “Club Med” party in Edward S. Harkness Hall, featuring the band Plato’s Cavemen, kicked off a week of auction activities that have replaced the free-standing event of years past. It netted \$630, including the \$210 paid for Stewart’s tie.

New activities this year also included a tag football game pitting first-years against second-years, a relocation of the

silent auction to the lobby in front of the Cushing/Whitney Medical Library and a new master of ceremonies, Frank J. Bia, *m.d.*, professor of medicine (infectious disease) and laboratory medicine. Quick with a quip, Bia brought down the house more than once with his jokes about items for sale. Stewart’s offer of a beef ‘n beer dinner for eight brought this from the emcee: “This just in. The *cdc* called this morning. They are classifying this as a level-four bioterrorist event.” When Herbert Chase, *m.d.*, deputy dean for education, offered a behind-the-scenes tour of the Museum of Natural History in New York, Bia joked, “You don’t have to go to a faculty meeting to see dinosaurs.”

Held November 15, the auction raised \$30,000 for several New Haven organizations that help the poor and the homeless. Proceeds went to New Haven Cares, Loaves and Fishes, New Haven Homeless Resource Center, Douglas House, Downtown Evening Soup Kitchen, Moore House Soup Kitchen and New Haven Home Recovery. This year’s highest-selling item was a weekend at second-year student Dave Aversa’s Vermont ski condo, for \$1,700. Dean David A. Kessler, *m.d.*, paid \$900 for two roles in the second-year show. Silent auction items included dinners, desserts, paddling and sailing outings, rides in airplanes, works of art, 20 hours of carpentry, massages, baby-sitting and dog walking.

First-year students won the football game, 26-22, and the game raised \$700 for charity. Students dedicated the game to Dean Emeritus Gerard N. Burrow, *m.d.* ’58, *hs* ’66, who has been appointed president and *ceo* of the Sea Research Foundation Inc., the not-for-profit organization overseeing Mystic Aquarium & Institute for Exploration. (See *Alumni Notes*, page 45.)



JOHN CURTIS (3)

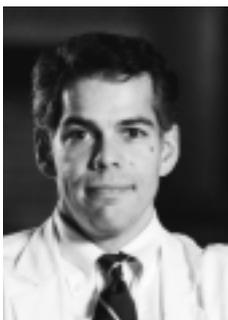
One of several new activities at this year’s fund-raiser was a tag football game between first- and second-year students that netted \$700 for the Hunger and Homelessness Auction. First-year public health student Derek Boucher lunges forward for a touchdown (top), while second-year medical student Jason Griffith tries to block his advance. At a half-time ceremony (middle), Dean David Kessler cited the accomplishments of Dean Emeritus Gerard Burrow (left), to whom the game was dedicated.



Francis Coughlin Jr.



Donald Moore



Francis Lobo

FROM DOCTOR TO LAWYER—AND NOW THE PRESIDENCY

New alumni leader hopes to build bridges across gender, the generations, and from academe to the community.

When **Francis R. Coughlin Jr., *m.d.* '52**, decided to quit surgery at age 58, he reinvented himself as a medical malpractice lawyer. He gets some grief about it from other physicians, but Coughlin has enjoyed learning how lawyers think. And medicine remains his first love.

As the new president of the Association of Yale Alumni in Medicine (***ayam***), Coughlin hopes to investigate how medicine can incorporate the needs and perspectives of women, who constitute more than half of the current first-year class at the School of Medicine. Coughlin, who succeeds Past President **Gilbert F. Hogan, *m.d.* '57**, also hopes to strengthen ties between Yale and community hospitals in Connecticut and to foster links between new graduates and older alumni.

Coughlin trained as a cardiothoracic surgeon, taking part in the first open-heart surgeries at Massachusetts General Hospital in the late 1950s. He spent 25 years in private practice in Stamford, Conn., raising eight children with his wife, Barbara Blunt Coughlin, ***m.d.* '52**, a medical school classmate. When a cataract in one eye marred his depth perception in 1985, he left surgery.

Since graduating from the University of Bridgeport School of Law at age 61, Coughlin has consulted with Connecticut attorneys for insurance companies that defend physicians and advised a New York law firm that prosecutes them. He evaluates cases for their merits and plans strategy but does not litigate. Since 1990, he has been vice-chair of the

Connecticut Commission on Medico-legal Investigations, which oversees the Office of the Chief Medical Examiner. When he became an attorney, Coughlin was intrigued by the different modes of thought used by doctors and lawyers. He says doctors make decisions based on a “convergence of probabilities,” discarding facts that seem irrelevant. Lawyers, on the other hand, “align all the facts in parallel lines of argument—the prosecution argument and the defense argument. ... A lawyer could move from the plaintiff’s side to the defense side and not miss a beat.

“I think of myself as a physician first and always,” says Coughlin, 75. “Medicine is a very fine way to spend a lifetime. It makes a real difference in the lives of people. In the law, in the civil justice system, the remedy for legal wrongs is monetary.” Yet, he adds, “The medical malpractice system is very important, and it is important that it be used properly.”

As ***ayam*** president, Coughlin plans to study how women are affecting medicine. “We are going to have to design the curriculum and develop expectations of physicians based on those who serve as physicians, so let’s find out about the role of women in medicine,” he says. Coughlin believes that women have taught men new approaches to teamwork. From women, he says, “we have learned more and more how we depend on each other. We have learned that it’s important to share information, to arrive at consensus.”

“MY VOCATION IS MY VACATION”

ayam Vice President **Donald E. Moore, *m.d.* '81, *m.p.h.* '81**, practices family medicine in Brooklyn, N.Y., concentrating on diabetes, ***aids***, asthma and hypertension—“the diseases of our population.” He even makes house calls. Moore describes reunions with senior faculty at alumni events as “a contemporary connection to the giants in medicine because they really have a lot of collective wisdom and individual wisdom.” Moore says the old-timers know that medicine has not always been—and will not always be—governed by the “contemporary wisdom” of efficiency above all.

Moore is interested in cultural differences — “how the culture of the individual you’re treating impacts on their health and their care and the relationship you are about to have. It’s very important. ... Half of medicine is an art. That takes time, you know. You can’t push the artist.” Moore enjoys family activities with his wife, Christine Moore, and their two daughters, but otherwise, he says, “my vocation is my vacation.”

Francis M. Lobo, m.d. ’92, *ayam* secretary, hasn’t really left New Haven since medical school. He did his residency at Yale and is now an assistant professor of medicine at Yale, doing basic research on gene activation in the immune system. He also works at the Dana Clinic, where he treats patients with allergies and immunological problems.

Lobo considers his Yale classmates “the nicest, smartest, kindest and gentlest people I’ve known.” He says the medical school manages to admit high achievers “who can adapt to an environment in which you’re asked not to compete, but to work together and to help one another, within a mature, graduate school ethic.”

NEW COMMITTEE MEMBERS

New members of the executive committee are **Cynthia B. Aten, m.d.** ’81; **Sharon L. Bonney, m.d.** ’76; **Joseph F.J. Curi, m.d.** ’64; **David H. Lippman, m.d.** ’71; and **Harold R. Mancusi-Ungaro Jr., m.d.** ’73, *hs* ’76.

Aten is a pediatrician who served as chief of undergraduate medicine at Yale for seven years. She is now studying how to augment the treatment of adolescent eating disorders using Reiki, an ancient system of healing touch. As a medical student, Aten appreciated the school’s flexibility, which allowed her to extend her clerkships over two years to see more of her two young children. She lives with her husband, Raymond Aten, in Hamden, Conn.

After studying engineering at Duke, Bonney used the Yale System to get the liberal arts education she’d missed. “I like to say I minored in English in medical school. ... I adore the Yale System

and I adore Yale.” Currently at Pfizer in New London, she is running trials of a cardiac drug. Bonney lives in Old Lyme, Conn., with her husband, James Beattie, and has three stepsons.

For 32 years, Curi has taken care of children and teenagers in the small city of Torrington, Conn., practicing solo. He likes preadolescents, “because you can still communicate with them.” He and his wife, Susannah Curi, have four children (two of them Yale College grads). Curi says that “because of the Yale System, I was really able to become a human being,” with time for sports and volunteer work. He’s served the *ayam* off and on for 20 years. “Working for Yale is not a chore, believe me,” says Curi.

Lippman has practiced psychiatry for two decades in Great Barrington, Mass. He worked as a doctor in Africa for two years in the mid-70s, and six years ago he and his wife, Honey Sharp Lippman, took their three children around the world (See *Books*, page 12). Lippman valued the noncompetitive atmosphere at Yale. “You were all in it together.”

Mancusi-Ungaro had planned to join his father as a pediatrician in New Jersey until his first clinical rotation, when he observed a surgeon repair a child’s fusion defect of the head. “What I saw was instant gratification,” recalls Mancusi-Ungaro. He was sold on surgery from that moment. Now he does plastic and reconstructive surgery in Beaumont, Texas. A “Texan by choice” (with pickup truck), he does come East to visit his two children at Yale College. “Yale is never out of your bloodstream,” he says.

New representatives to the Association of Yale Alumni are **Arthur Ebbert Jr., m.d.**, and **Betty R. Klein, m.d.** ’86, *hs* ’91. Ebbert studied medicine at the University of Virginia and came to Yale in 1953 as an instructor. He served as deputy dean of the medical school beginning in 1973. The *ayam* made Ebbert an honorary alumnus when he retired in 1988. He sold his sailboat, Goose, last year, but still sails with friends. Klein is an ophthalmologist in Danbury, Conn., specializing in the retina. She and her husband, Eric Yale Brown, have two children.



Cynthia Aten



Sharon Bonney



Joseph Curi



David Lippman



Harold Mancusi-Ungaro Jr.



Arthur Ebbert Jr.



Betty Klein

A YALE COUPLE, FACING POLIO, FOUND THEMSELVES “CALLED TO RISE”

“The city streets were deserted at 11:30 p.m. It was a balmy spring night in 1945 when my husband, Larry, and I set out for a walk after work [at the New Haven Hospital]. Larry was a surgical intern and I was a student nurse and I had just come off duty on the evening shift.”

So begins *Called to Rise: A Journey Through Disability*, Madeleine Crowley’s memoir about a life changed by polio. A little more than three years after this spring stroll, she lay gravely ill in the hospital where she had worked, fearing for her life and for the future of her husband, a 1944 graduate of the School of Medicine, and their two-year-old son. In the months and years that followed her hospitalization on Thanksgiving Day 1948, Crowley overcame most of the obstacles presented by the disease. She decided to write the book, published last May by Western Book/Journal Press in Reno, Nev., to inspire others with disabilities.

Lawrence and Madeleine Crowley met as students on the medical ward on Fitkin 1 during the war years. In mid-November 1948, their only child, Lawrence Jr., became infected with the polio virus but recovered fully. Madeleine’s case was much more serious. After a week of intermittent consciousness, she awoke to discover that she had lost the use of her arms and legs. Despite several weeks of difficult breathing, she managed to avoid the iron lung, and early the next year began rehabilitation in Warm Springs, Ga., in a hospital designed by its most famous patient, President Franklin D. Roosevelt.

The book’s title refers to a line in the first stanza of an Emily Dickinson poem: “We never know how high we are/Till we are called to rise:/And then, if we are true to plan,/Our statures touch the skies.” During that balmy spring walk in 1945, Madeleine Crowley told her husband that she wanted to live life to the fullest, and it was a promise that she kept. She regained partial use of her limbs and learned to walk on crutches

before post-polio syndrome required her to use a wheelchair years later. She gave birth to two more children, Suzanne and Stephen, and ran the household as the family moved first to California, then Wisconsin. When the children grew up and left home, she went back to work, first as a hospital volunteer, then as a career counselor.

From time to time, she said in a phone interview from her home in Cupertino, Calif., “I would feel a flood of sadness come over me and I’d wish life had been different. But there were so many things I wanted to do and the world was out there waiting. I’d say, ‘Oh the heck with it. I’m not going to let it stop me.’”

The same was true for her husband, who thrived despite the initial interruption in his career as an academic surgeon. Lawrence Crowley, *m.d.* ’44, *hs* ’51, scrambled to find a fellowship at Emory while Madeleine was in Warm Springs, then returned to Yale for two years to serve on the faculty. In 1953, the harsh New England winters drove the family to the easier climate and lifestyle of California, and Lawrence briefly left academic medicine for private practice in Los Angeles. Before long he joined the faculty at Stanford, rising to become dean of the medical school and vice president of the university. From 1974 to 1978, he served as dean of the University of Wisconsin Medical School.

“It turned out to be a very wise move,” Lawrence Crowley said of the difficult decision to leave New Haven. “If things had been different, I might well have stayed at Yale and still be there today. But Madeleine was much more independent in California. And we had a great time.”



MICHAEL FITZSOUSA (2)

A BIG HELLO IN MUSIC CITY

Victoria Holloway, *m.d.* ’94 (above, left), and Pamela Perry, *m.d.*, a former Yale faculty member in emergency medicine, catch up on news during an alumni reception at the National Medical Association meeting in Nashville in August. Among those attending the reception were Perry’s brother, Victor Perry, *m.d.* ’93, and (top) Mary Kathleen Figaro, *m.d.* ’96, and Owen Garrick, *m.d.* ’98. The Association of Yale Alumni in Medicine hosted get-togethers for alumni in New York City, Vero Beach and Ft. Lauderdale in January and Boston in February and will hold events in Chicago, Texas and California in March and April. For an updated schedule, see info.med.yale.edu/ayam/news.html.



Madeleine and Lawrence Crowley

NOTES

1940s



JOHN L. CANNON, M.D. '47, of West Simsbury, Conn., who retired from active practice in 1998, writes to say that his 43-year-old daughter, Cecily, a paramedic and firefighter, entered the University of New England College of Osteopathic Medicine in Biddeford, Maine, in August. He also has two sons: Jack, who works in the Hartford office of the New York investment firm Roosevelt & Cross Inc., and Andy, who teaches marketing at the University of South Alabama. Cannon has nearly completed the restoration of a 50-year-old wooden sailboat and writes that he has two others yet to do, as well as other projects too numerous to mention.

1950s



Dean Emeritus **GERARD N. BURROW, M.D.** '58, HS '66, has been named president and CEO of the Sea Research Foundation, the not-for-profit organization that oversees Mystic Aquarium & Institute for Exploration. Burrow will work to extend the foundation's mission of "education and research, with entertainment at the center" by supporting new technologies to bring the experience of the sea to people on land. Burrow was an intern and resident in internal medicine at Yale, and a fellow here in endocrinology. He served on the Yale faculty before becoming the Sir John and Lady Eaton Professor and chair of medicine at the University of Toronto, then vice chancellor and dean of the University of California San Diego School of Medicine. Burrow was dean of the Yale School of Medicine from 1992 to 1997.

1970s



GEORGE J. DOHRMANN, M.D., PH.D., HS '78, a neurosurgeon at the University of Chicago Medical Center and a member of the faculty at the Brain Research Institute in Chicago, received the 2001 Bucy Award in recognition of his outstanding contributions to neurosurgical education, both nationally and internationally. The award honors teacher and neurosurgeon Paul C. Bucy, M.D., who lived from 1904 to 1992. Bucy collaborated on research in neurophysiology with John Fulton, M.D., at Yale before returning to Chicago, where he led the neurosurgery departments at the University of Chicago and Northwestern University.



LAWRENCE V. MEAGHER JR., M.P.H. '76, of Garland, Texas, president and CEO of International Hospital Corporation, was selected as a 2001 Wheeling Jesuit University (WJU) Distinguished Alumnus for his work in bringing health care to Third World countries. He is co-founder of the Dallas-based company, which specializes in developing and managing acute-care hospitals and other health services in Mexico and Latin America. Meagher said "lessons learned at WJU were central to [his] approach today—a concern for people and energy, persistence and integrity, in an atmosphere of constant challenge to the status quo."

1980s



The Tulane University Health Sciences Center has named **TYLER CURIEL, M.D., M.P.H.**, HS '86, as the new chief of the section of hematology-oncology at its school of medicine. Curiel, who holds the Henderson Chair in Medicine at Tulane, studied medicine at Duke and public health at Harvard and completed an internship and residency in internal medicine at Yale. He has an interest in developing therapies for cancers and infectious diseases by boosting the body's immune system. He holds four patents and has more pending for novel therapies in these areas.

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

2001-2002

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Jocelyn S. Malkin, M.D. '51, HS '52

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ROBERT W. BERLINER, M.D., professor emeritus of cellular and molecular physiology and a former dean of the School of Medicine, died on February 5. He was 86.

Berliner came to Yale in 1973 after a distinguished career at the National Institutes of Health (NIH), and for the next 11 years guided the school as it became one of the country's leading research institutions. He was well known for his contributions to the study of renal physiology and was a leader in shaping American biomedical science. With colleagues, he was instrumental in elucidating the main features of potassium excretion by the kidney.

A native of New York, Berliner graduated from Yale College in 1936 and studied medicine at Columbia University. He did his residency at Presbyterian Hospital and Goldwater Memorial Hospital in New York, and began his research career at Goldwater. In 1950 he left Columbia, where he was an assistant professor of medicine, for a job at the NIH. There, he built the Laboratory of Kidney and Electrolyte Metabolism and served as its chief for 12 years. He subsequently became director of intramural research at the National Heart Institute and deputy director for science at the NIH.

He was a member of the National Academy of Sciences and of the Institute of Medicine. At Yale he was honored by the creation of the Robert W. Berliner Chair and the Robert W. Berliner Lectureship in Renal Physiology.

ALLEN CHETRICK, M.D., '53, HS '56, former associate clinical professor of medicine at Yale, died of cancer in Branford, Conn., on October 2. He was 74.

Born in New Haven, Chetrick graduated from Yale College in 1950 and from the School of Medicine three years later. He served an internship in medicine at Bellevue Hospital in New York City and two years of residency at the West Haven Veterans Administration Hospital and Grace-New Haven Community Hospital. The American Heart Association awarded him a research fellowship in cardiology in 1956.

Chetrick joined the Yale faculty in 1957 and practiced internal medicine and cardiology in New Haven for 41 years. He was an attending physician at Yale-New Haven Hospital and The Hospital of St. Raphael. Chetrick also served in the Navy during World War II. He was a fellow of the American College of Physicians and a member of the American Society of Internal Medicine. He was also past secretary of the internal medicine section of the Connecticut Medical Association.

In 1969 Chetrick received the Israel Service Award from the Greater New Haven Israel Bond Committee.

ALVAN R. FEINSTEIN, M.D., HS '54, Sterling Professor of Medicine and Epidemiology, died of a heart attack at an awards ceremony in Toronto on October 24. He was 75.

A native of Philadelphia, Feinstein received his bachelor's degree, a master's degree in mathematics and his doctor of medicine degree from the University of Chicago. He completed his clinical training in

internal medicine at Yale and his research training at Rockefeller Institute. Feinstein joined the Yale faculty in 1962 and became the founding director of the Robert Wood Johnson Clinical Scholars Program at Yale in 1964. Under his direction, the program became recognized as one of the leading sites for training in the methods of clinical research. He was also the director of the clinical examination course (for second-year medical students) and created a course in quantitative clinical epidemiology (for Johnson Clinical Scholars) that was imitated throughout the country.

Because of his work on the statistical analysis of clinical signs and symptoms of real patients—rather than on the historically nonclinical methods of pure statistics—Feinstein was a key figure in the establishment of the field of clinical epidemiology. His approaches and methods were reported in three books: *Clinical Judgment*, *Clinical Epidemiology* and *Clinimetrics*. His approaches to quantitative data were presented in three other books: *Clinical Biostatistics*, *Multivariable Analysis* and *Principles of Medical Statistics*. Feinstein will be remembered for his influence on the careers of over 100 fellows who trained in the clinical scholars program and others who considered him their intellectual muse.

MONTE NELSON FRAZIER, M.P.H., '65, of Colebrook, Conn., a graduate in epidemiology and public health and a veterinarian, died June 29 at the age of 76.

Frazier, as noted in an obituary in *The Hartford Courant*, had a worldwide reputation in an esoteric specialty, the health of poultry. He parlayed a boyhood chore on his father's Michigan farm into an international career. Frazier

taught in the agriculture department of the University of Connecticut, then joined Arbor Acres Farm Inc. in Glastonbury, Conn., serving as director of poultry health for 25 years.

He was an early advocate for using the highest standards of cleanliness and sanitation in order to eliminate diseases that could decimate whole flocks. He thought the best precaution was to isolate the birds from humans, other birds and animals.

Frazier, known from Venezuela to India, worked for Aviagen Inc. (formerly Arbor Acres Farm Inc.), a company that does business worldwide. He logged up to 100,000 miles a year, to 35 countries in all, visiting farms and giving lectures on disease prevention. At the end of his career, Frazier lectured in Thailand to poultry experts whom he had helped train over several decades.

C. NORMAN GILLIS, PH.D., professor emeritus of anesthesiology and of pharmacology at the School of Medicine, died in Boston on August 16. He was 68.

Gillis, a native of Scotland, earned his PH.D. degree in 1957 from Glasgow University. He came to Yale in 1961 as assistant professor of pharmacology. In 1966 he was named associate professor of pharmacology, and in 1969, associate professor of anesthesiology. In 1973 Gillis was named professor of anesthesiology and of pharmacology, and served as director of anesthesiology research from 1979 until 1993.

Gillis, nationally recognized as a specialist in pulmonary vascular disease and pharmacology, published more than 250 scientific articles during his career. He had recently been appointed to serve on a committee of the Institute of Medicine and was an adjunct pro-

fessor of medicine at Tufts University School of Medicine. He was an associate editor of the journal *Biochemical Pharmacology* and served on the editorial boards of several other journals in his field.

RICHARD H. GRANGER, M.D., HS '51, of Guilford, Conn., a member of the faculty in the Child Study Center, an advocate for children and a former master of Morse College, suffered with multiple myeloma and died of pneumonia on April 9 at Yale-New Haven Hospital. He was 76.

While at Yale, Granger sought to train pediatricians to understand the interface between physical and psychological development. He established a program for the continuing education of pediatricians that brought them together with child psychiatrists to address the challenges faced by children and families. Granger had his own pediatric private practice in New Haven before joining the Child Study Center in 1969, where he supervised three major facilities expansions and served under three of the Center's four directors. He was master of Morse College from 1975 to 1982.

Granger served as president of both New Haven's Dixwell Community House and the New Haven Area Mental Health Association. He headed the research unit of Connecticut's Mental Health Association, and was also a delegate to the White House Conference on Children.

LAURENCE VAN DOREN HARRIS JR., M.D. '51, formerly of Thomaston, Conn., died of spinal cancer on September 7 in Longwood, Fla. He was 78.

Harris was born in Wallace, Idaho. He attended high school in

Kent, Conn., and completed one year at Williams College in Williams-town, Mass., before enlisting in the Army during World War II. He returned to Williams after the war to complete his bachelor's degree and then received his medical degree from Yale. Harris served his internship and residency at Waterbury Hospital, and after four years in private practice in Thomaston, he returned as a surgeon to the Army Medical Corps with the rank of major. Harris served in the United States, Germany and Thailand and completed his 20 years of service as a colonel before retiring to Florida.

JEROME K. MYERS, PH.D. '50, a retired Yale sociology professor and pioneer in the fields of social psychiatry and medical sociology, died May 7 at the age of 79.

Born in Lancaster, Pa., Myers graduated from Franklin and Marshall College in 1942 and served in World War II before earning his master's and doctoral degrees in sociology at Yale.

Myers remained at Yale throughout his 43-year career of teaching and research. During that time he co-founded and directed a National Institutes of Mental Health training grant program in medical sociology.

Myers was principal investigator of a number of large-scale community surveys on mental health and mental health services, which culminated in the first major study of the prevalence of mental disorders in the United States. He authored and co-authored many books, including *Research Techniques in Schizophrenia*; *Family and Class Dynamics in Mental Illness*; *A Decade Later: A Follow-up of Social Class and Mental Illness* and *Community Surveys of Psychiatric Disorders*. Among Myers' honors were the Rema Lapouse Award from the American

Public Health Association and the Distinguished Career Award from the Psychiatric Sociology Section of the Society for the Study of Social Problems.

RAYMOND E. PARKS, M.D. '45, died August 9 at his home on St. Simons Island, Ga., at the age of 78.

Born in St. Paul, Minn., Parks received his medical degree from Yale and was awarded the Campbell Prize, which is given to the student obtaining the highest standing in medical studies. He served his internship at Ramsey County Hospital in St. Paul, followed by a tour in the U.S. Army Medical Corps, where he attained the rank of captain. He completed his residency at Johns Hopkins Hospital.

Certified in radiology and nuclear medicine, Parks was a consultant for the Florida State Board of Health. He was appointed to the Florida Air Pollution Control Commission in 1960, serving until 1967. He was also a radiologist on the heart transplant team at Cape-town University in South Africa during 1968. Parks was a member of the National Advisory Council on Radiation in Washington. He served as associate dean for continuing education at the University of Miami (UM) and professor and chair of the Department of Radiology at the UM School of Medicine.

During his career Parks also served as director of radiology at Jackson Memorial Hospital in Miami, Kendall Hospital, Cedars of Lebanon Hospital, National Children's Cardiac Hospital, Broward General Medical Center, North Broward Hospital and Imperial Point Hospital. He retired as clinical professor of radiology at the University of California at Davis.

ROBERT R. WAGNER, M.D. '46, of Charlottesville, Va., professor emeritus of microbiology at the University of Virginia Medical School, died of lung cancer on September 15 at the University of Virginia Hospital. He was 78.

A native of New York and a 1943 graduate of Columbia University, Wagner taught microbiology at Yale and Johns Hopkins before moving to Charlottesville. He was on the faculty at Yale as an instructor in medicine from 1951 to 1953 and as an assistant professor of medicine from 1953 to 1955.

Wagner joined the University of Virginia faculty in 1967 as chair of the microbiology department and remained chair until 1996. He was founding director in 1983 of the school's cancer center and served in that position until 1995.

He co-edited the multivolume texts *Comprehensive Virology* and *The Viruses* and published more than 200 articles in scientific journals. Wagner was a president of the American Society for Virology and a diplomate of the American Board of Internal Medicine.

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

Moving beyond fear *continued from page 22*

talking about high-risk groups, instead of high-risk behavior, have led to the idea that *hiv* is for someone else: for sex workers, truck drivers or “immoral” people. Too many people have decided they simply aren’t at risk. We’re trying out a method of measuring an individual’s perceived distance from the epidemic based on the kinds of questions he or she asks—a “Continuum of Enquiry.” Designed as a matrix, on the far left is someone who feels far from the epidemic and at virtually no personal risk. On the far right is someone living with *aids*. In between are people practicing multipartner sex, people who have contracted a sexually transmitted infection, people who are contemplating a test and people who are living with *hiv*. Moving from left to right, the questions become more detailed, heartfelt, and personal, and the person’s risk perception increases. As a person feels closer to the epidemic, the possibility of behavior change should increase as well.

For example, a person who asks, “Can mosquitoes transmit *hiv*?” or “What is the shape of the virus?” probably does not feel at great personal risk. But someone who asks, “If you’ve had gonorrhea, does that put you at risk for *hiv*?” may be feeling a little closer to the reality of the epidemic. And when a child asks, “Why are people with *aids* so harsh?” we can feel sure he or she has had personal experience. The key is to help the child use that experience to think about risk, protection and a future free from *hiv*.

At the Westlands roundabout, the traffic has degenerated into merry chaos behind us and the traffic cop is still asking questions—relatively superficial ones according to our matrix, but questions just the same. After a few minutes, he gives us a last probing look, then stops traffic and waves me through.

In the two years I’ll spend here, I can’t really expect to see a noticeable change in the *hiv* incidence rate, and even if I did I would be hard pressed to say I had contributed to it. But I know that one policeman learned a few things he didn’t know before, and asked some questions that may have made him think. He might talk to others and raise a few questions in their minds, and as they search for the answers they may change their risk perception. I have to believe that every little bit helps. And I *did* manage to dodge the traffic ticket. **YM**

KAREN SCHMIDT, M.P.H. ’00, worked as a journalist for 10 years before coming to Yale in 1997 as a student in the School of Public Health. She can be reached by e-mail at karens@aya.yale.edu.

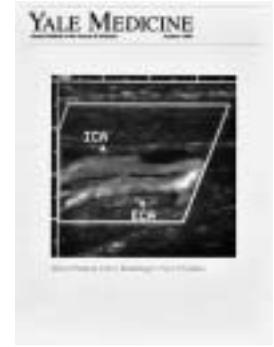


FROM “ANATOMY DEMONSTRATIONS TELECAST” IN THE WINTER 1966 ISSUE: “Among the many things in life and art that will never be the same as they were before television is the projection of the infratemporal fossa.

Formerly, when first-year medical students at Yale watched anatomy dissections in groups of 12 or 14, it was possible for only one student in each group (or two at the most, forehead to forehead) to peer directly into the three-inch-deep infratemporal cavity while the instructor identified and explained its parts. The others in the group, unable to see what was being demonstrated, could only try to visualize and commit to memory the divisions of the trigeminal nerve and the branches of the maxillary artery.

The close view that was once available to only a few students is now shared, via closed circuit television, by 80 students simultaneously, each of whom benefits to a far greater degree than before.

Because the demonstration is recorded on videotape, it can be repeated as many times as one or more students wish to study it while performing their own dissections.”



FROM “THE MIND OF THE TERRORIST” BY JERROLD M. POST, M.D. ’60, SUMMER 1989: “While the public regularly assumes such bloodshed can only be the product of crazed minds, the acts of crazed fanatics, most terrorists do not suffer from serious (Axis I) mental disorders; indeed, psychotic disorders would be incompatible with the level of planning and group cooperation required to carry out sophisticated terrorist action. Moreover, behavioral scientists ... have not succeeded in identifying a unique ‘terrorist mindset,’ a particular psychological type, a particular personality constellation.

But while there is a diversity of personalities attracted to the path of terrorism, individuals with particular personality traits and tendencies are drawn to terrorist careers. One pattern frequently described resembles the sociopathic personality—action-oriented, aggressive individuals with a diminished capacity for empathy, who are stimulus-hungry and seek excitement. Another type is the angry paranoid, ready to lash out at his enemies—real and imagined. ...

As the product of generational forces, political terrorism will be here for generations to come. *There is no short-range solution to this problem.* In the long run, the most effective ways of countering terrorism are to reduce external support, to facilitate pathways out of terrorism, and, most importantly, to reduce the attractiveness of the terrorist path for alienated youth.”

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