

Yale Medicine

spring 2004

Marie Curie's historic
day at Yale

16

Memories from the
heart of Harkness

18

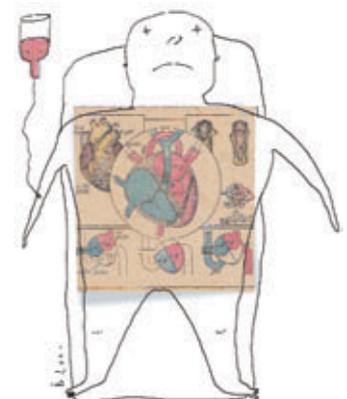
A research partnership
in Tehran

24

he had vital signs, he was hemor-
rhaging rapidly through the wound.
There was wide destruction of his
brain tissue. My immediate reaction
was, "This poor person has died." Any
intervention at that point seemed
futile. Then another doctor who was
present ordered blood. I was shocked
and asked, "Why?" The doctor replied,
"Perhaps he will be an organ donor."

A question of ethics.

page 30





SPRING 2004

CONTENTS

ON THE COVER

Ethical quandaries can leave clinicians and scientists uncertain as to the best way to proceed. Starting on page 30, Yale faculty experts in bioethics respond to real dilemmas posed by our readers. *Illustration by Serge Bloch*

- 2 **Letters**
- 4 **Chronicle**
- 10 **Rounds**
- 12 **Findings**
- 14 **Books**
- 15 **On Campus**
- 16 **Capsule**

- 18 **“That college feeling”**
What student in her right mind would spend four years in a dorm? Ask Jenny Blair, who enjoyed a gym in the basement, a piano in the ballroom and snowball fights right outside the door.
By Jenny Blair

- 24 **Journey of the heart**
A collaborative bridge between Yale and Iran spanning the genetics of cardiovascular disease is a two-way street for science.
By Trisha Gura

- 30 **Two alternatives, each a little wrong**
With that definition of a dilemma in mind, Yale’s cadre of bioethicists waded into our mailbag and weigh in on readers’ questions from the front lines of medicine.
By Marc Wortman

- 38 **Faculty**
- 39 **Students**
- 42 **Alumni**
- 47 **In Memoriam**
- 48 **Follow-Up**
- 48 **Archives**

On the Web

info.med.yale.edu/yym

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

“I loved medicine but do not miss it”

The following is a response to a letter from Howard Spiro, M.D., that appeared in the Autumn 2003 issue of Yale Medicine.

Dear Howard,
That you should respond to my essay with a letter half again as long as that to which you responded [“Knowing When It’s Time to Quit,” Summer 2003] brings to mind G.B. Shaw’s coda to a letter, “Forgive me for writing a long letter but I did not have time to write a short one.” My response to you will be shorter.

My two main reasons for retiring are relevance to my medical community and lack of an adequate intellectual schema in which to incorporate new knowledge. I was bothered by the impending irrelevance that I had seen afflict older physicians. Friends of mine, particularly doctors and attorneys, concur in the recognition. Does being troubled by that prospect reveal inadequate ego strength or simply an accurate perception of reality? Choose one!

The problems of understanding and incorporating new knowledge and its effect on how I wanted to practice are linked to your statements about continuing to practice in a changed capacity and the wisdom that comes to some with age. All the kindness and wisdom in the world are not, in my opinion, worth much if not backed by up-to-date knowledge. I suspect that doctors who practice part time in clinics after retiring are not offering first-rate medicine.

You take me to task for not being a “mid-1930s liberal.” I plead guilty. The implication

that somehow it was immoral to retire and deprive the world of my (supposed) talents is a bit harder to take. Perhaps I should have spelled out my thoughts more clearly. For me to continue to practice and encounter the loss of respect of my colleagues—and your colleagues know you better than you know—and be unable to use new information properly would have been to practice under false pretenses.

Do I think everyone should retire at a specific age? Of course not. With rare exceptions, however, there comes a time when older physicians should make way for younger ones. I chose what I chose. I make no apologies. I loved medicine but do not miss it. I am very happy in my current state.

Your longtime friend and student,

*Herbert J. Kaufmann, M.D. '59
Bedford, N.Y.*

For more on this topic, see the online Yale Journal for Humanities in Medicine at info.med.yale.edu/intmed/hummed/jjhm/.

Strong support from chief helped female surgeons

I read with interest the article on the growing number of women in surgery [“Closing the Gender Gap,” Winter 2004] and was pleased that Barbara Kinder mentioned William Collins as one of those who strongly supported women in the surgery program. As the first woman resident in neurosurgery at Yale (and the third to be board-certified in the country), I was fortunate that Dr. Collins literally “took a chance” and accepted me on the resident staff. I recall early in my residency when the chairman of one of the major neurosurgery departments in the country said to Dr. Collins (in a voice calculated to reach me), “Bill, I thought you came here to build a first-rate program. How do you expect to do that after you bring a woman on staff?” Dr. Collins’ support was invaluable not only during residency and when I was a faculty mem-

ber, but later in my career as well. Thanks, Barbara, for remembering.

I would also like to echo Dr. Kinder’s reservations about the reduction in resident duty hours. As one who attended a medical school in New York with a county hospital affiliation, I know it was not necessarily the fatigue of house staff that caused the errors that aroused the concern of legislators, but the inability to get senior staff to respond to night call. For example, in my third-year obstetrics rotation I delivered more than 30 babies, and I was “taught” to do pudendal blocks (among other things, like breaking a clavicle for a shoulder dystocia) by the night nurse. I agree with Dr. Kinder that the diffusion of responsibility that occurs with the shortened hours is a significant negative. And perhaps more importantly, it will do little to solve the problem.

*Joan Venes, M.D., HS '67
Sacramento, Calif.*

Cos, not Ephesus, was Hippocrates’ birthplace

In reference to the caption under the photo of a sycamore tree on Harkness Lawn [“A Nurturing Vision,” Winter 2004], Hippocrates was not born in Ephesus, but rather on the island of Cos off the Ionian coast.

*William B. Radcliffe, M.D. '58
Mitchellville, Md.*

Dr. Radcliffe is correct. Due to an editing error we stated the incorrect birthplace for Hippocrates.



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.

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Connective tissue

I still have vivid memories of my first day of dorm life. The year was 1977, the city was Baltimore and the weather was what you'd expect in late August: hot and very humid. Music filled the quad, and there was a communal air that endured long after we had moved off the Hopkins campus for the thrill of living on our own.

That was Maryland, not Connecticut; college, not med school; but the experience held the same charm for me that Jenny Blair conveys in her memoir of life in Harkness Hall ("That College Feeling," page 18). Dorm life has its downside, but it's the one time many of us will live elbow to elbow with so many of our peers.

The "connective tissue" linking physicians is a thread in our cover story about the dilemmas doctors face. The values instilled by institutions such as Yale and reinforced by the relationships that begin here form the basis for ethical decision making for years to come. Our third feature describes yet another kind of connection, this one a collaboration between physicians in New Haven and Tehran that revealed the genetic cause of a cardiac disorder.

To meet our goal of keeping the Yale family in touch, we rely on you, our readers, to share stories of interest to your colleagues, friends and former classmates. Whether it's a brief note for the Alumni section, a profile suggestion for *Faces* or a larger story, we'd like to hear about it. Drop us a line the next time you feel like connecting.

Michael Fitzsosa
michael.fitzsosa@yale.edu

SECOND OPINION BY SIDNEY HARRIS



Health care van rides a road less traveled

For city residents with limited access to medical services, Yale's mobile clinic fills a critical void.

The Community Health Care Van parks in front of an apartment house with plywood nailed over the windows. Orange spray paint on the Congress Avenue tenement demands, "Whose Livable City Is This?"—a reference to New Haven's anti-blight initiative. It is cold and rainy, the kind of weather that discourages patients from venturing out to the mobile clinic. But enough people show up to make for tight quarters.

Joel stoops to walk inside.

"It's a good day because we're alive to see it," the lanky man says with a grin as he brushes raindrops from his jacket.

This is an optimistic time in Joel's life; with the assistance of the van staff, he has just signed up for substance abuse treatment. But first he needs a physical and a tuberculosis test, and the van takes walk-ins. Waiting weeks

or even days for an appointment at a clinic would be difficult and risky for a man who says he is "just trying to find the strength one day at a time."

Entering its 10th year of service to New Haven, the van has always emphasized free, immediate and dignified care, says Frederick L. Altice, M.D., HS '89, associate professor of medicine (AIDS Program) and director of the Community Health Care Van initiative. Altice got the idea for a mobile clinic a decade ago while working with New Haven's needle exchange program. He saw people come in with abscesses that went untreated until they were acute enough to land the client in the emergency room.

With a small van borrowed from Yale-New Haven Hospital's Primary Care Center, Altice began following the needle exchange van once a week. Along with a social worker and HIV counselor, Altice provided primary care, mostly to injecting drug users. Today, a newer, 36-foot van serves patients 11 hours a day, five days a week throughout the city. The rotating

staff includes senior physicians, residents, HIV specialists, a nurse practitioner, a physician associate, an HIV counselor, a drug treatment coordinator, a case manager, outreach workers and a number of volunteers. Usually four staff members ride on most trips. Many others are immediately available by cellular telephone.

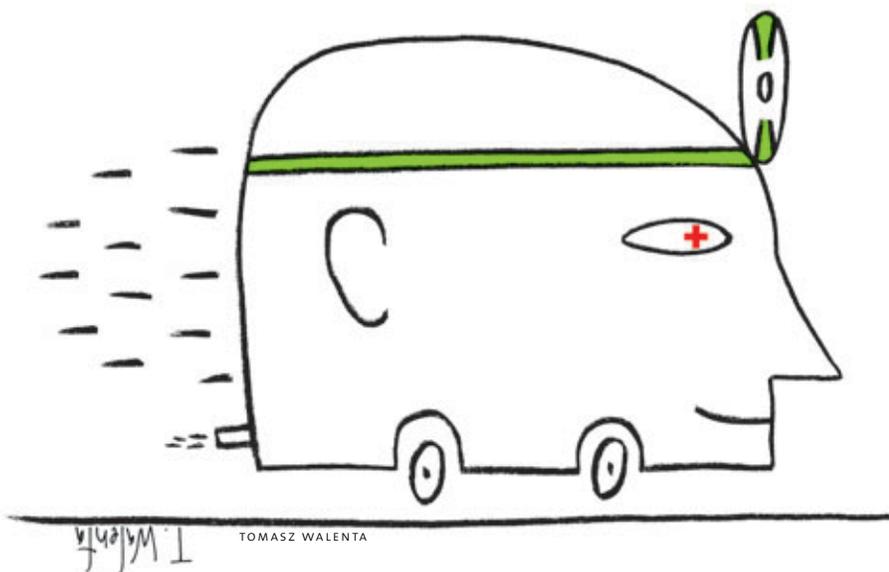
The van's impact on the community is well-documented: a 41 percent reduction in emergency department visits for clients who are injecting drug users, a 66 percent success rate in getting drug users to complete all three shots in the hepatitis B series, and promising results using buprenorphine to reduce heroin cravings. For clients who do not qualify for entitlements, the van may be their only treatment option. Where possible, the aim is to move the patient toward a community health center or some other fixed source of primary care. In 41 percent of the cases, that transition is successfully made. The van has done promising work on TB screening with undocumented residents, says Altice, which he expects to publish soon. Similar work is going on with the homeless.

About half of the 500 to 600 patients who visit the van each month arrive with issues unrelated to drugs. On the same morning that Joel needs a physical to get into treatment, a teenage girl with seashells braided into her hair, powder-blue tennis shoes and a handbag that says "Princess" takes a seat in the van. "I'm here for two reasons," she announces with studied nonchalance, "a pregnancy test and an HIV test."

Within minutes, she has seen a mental health counselor, a physician and an HIV counselor. She is relieved to get test results quickly and without a lecture. As she leaves with condoms she smiles and says, "I'll be seeing you."

"Everybody I meet on the van is always nice," says Michael, 28, who takes his daily HIV medications here. "This gets my morning going."

Much of the ongoing care the van provides also is the basis for research



that might help patients far beyond New Haven. Some clients take their HIV medications in the van as part of an effort to increase adherence. Data collected so far show that the directly observed medication program works, according to Robert Douglas Bruce, M.D., clinical instructor of medicine. Some patients, he says, have seen their viral loads fall and their T cells rise substantially. The research project is funded by the National Institute on Drug Abuse.

Research funding has largely sustained the van, says Altice. The mobile clinic is an ideal setting for many other investigations. For example, he is eager to monitor HIV therapy for inmates released from prison. HIV tends to be well-managed in prison, but viral loads often rise after release.

Aside from research grants, fundraising efforts have been difficult, Altice says, in part because the clientele arouses little public sympathy. It is precisely that lack of sympathy that the van staff is determined to combat. For example, many patients say they have been treated terribly by other health care providers, which makes them reluctant to seek treatment. Charly began coming to the van for primary care after her release from prison. Though she found work immediately after returning to New Haven, her job provides no health benefits. Charly says that on the van she gets a measure of respect she rarely finds elsewhere: "You don't have to be afraid to tell them about nothing," she says. Perhaps that's the secret of the van's success.

—Colleen Shaddox

Biomedical engineering becomes a department, uniting several disciplines

In eight years, biomedical engineering at Yale has grown from a fledgling undergraduate major to the university's newest department.

The Yale Corporation approved the formation of the interdisciplinary Department of Biomedical Engineering last summer with the participation of the medical school as well as the faculties of engineering and arts and sciences and the John B. Pierce Laboratory. Yale has offered an interdisciplinary program in biomedical engineering since 1996, led by James S. Duncan, PH.D., professor of diagnostic radiology, biomedical engineering and electrical engineering, but the decision to create a department signals how far the field has come. "I see a whole new set of symbiotic capabilities coming out of this partnership," said Paul A. Fleury, PH.D., dean of the Faculty of Engineering. These include the marriage of computer modeling of tissue mechanics with clinical practice, the application of computer technology to enhance imaging data from MRI, and techniques for using biologically compatible materials to deliver drugs or cells.

The department already has 70 undergraduate and 30 graduate students. There are nine primary and four secondary faculty members, with plans to fill three more primary faculty positions. Ongoing research projects include bioimaging and intervention in neocortical epilepsy, modeling of drug transport for brain tumor therapy, motor control in low-back injuries, and fMRI for neurosurgical planning in

epilepsy. The department is now housed in the Becton Science Center, but ground was broken in December for its new home in the Engineering Research Building on the corner of Prospect and Trumbull streets.

Fleury says the department is fully interdisciplinary, with several faculty members appointed in both the medical school and the Faculty of Arts and Sciences. "We expect that this arrangement will enable seamless relationships among the departments," he said.

W. Mark Saltzman, PH.D., chair of the new department, says the interdisciplinary environment and potential for collaboration are what drew him to Yale. Saltzman, who was previously at Cornell University, is working on drug delivery and tissue engineering. He says his top priorities as chair are to enlarge the faculty and to add new courses.

Fleury says the Yale program will succeed because it is closing a cultural gap. "Medical doctors often see engineers merely as gadgeteers who can supply methods or devices, but are not interested in or capable of engaging in the deeper roots of clinical and medical challenges," he said. "Conversely, engineers are often skeptical of doctors' scientific interests and depth. I am glad to say that these gap characteristics are vanishingly small here at Yale."

—Jennifer Kaylin



W. Mark Saltzman, chair of the new biomedical engineering department, and Erin Lavik, an assistant professor, with a sample of a polymer wafer capable of delivering therapeutic agents in the brain after surgery.

MICHAEL MARSLAND

Peter Fonagy, Mary Target and Yale professor Linda Mayes are the new directorial team at the Anna Freud Centre in London, which has long-standing ties to Yale's Child Study Center.



Renewed “vows” herald a stronger link between Yale and London

When a trans-Atlantic group of psychiatrists and psychologists gathered at Yale in early December, it was as much a reunion of old friends as an academic symposium at the Child Study Center. Many in the group have known each other for years. They have written papers together, mentored and trained each other and collaborated on research and interventions.

The reason for the symposium, “Developmental Science and Psycho-

analysis: Integration and Innovation,” was to formalize three decades of largely informal ties between Yale and the Anna Freud Centre in London. The symposium also celebrated the launching of the Anna Freud Centre Program at Yale and a revitalization of the Centre in London.

Alan E. Kazdin, PH.D., director of the Child Study Center, likened the celebration to the renewal of wedding vows. “There has already been a very enduring marriage that has worked out very well,” he said. “Let’s go through the ceremony and vows again and chart the future.”

What the future holds for Yale’s participation in the program is a series of exchanges that will bring students and scholars across the Atlantic for training, research and study. Linda C. Mayes, M.D., the Arnold Gesell Professor of Child Psychiatry, Pediatrics and Psychology in the Child Study Center, will head the program at Yale and is one of three members of a new directorial team that will lead the Freud Centre.

According to Mayes, the program at Yale will offer training that includes exchanges for scientists and scholars, a master’s program, an undergraduate program and an international visiting-scholar program. The program will also include joint research projects focused on the science of early attachments and emotional development. “The idea is to have a continual exchange of ideas and very active collaborative clinical research,” she said.

The exchanges between London and New Haven go back three decades. In the early 1970s, the late Albert J. Solnit, M.D., HS ’52, who headed the

Child Study Center from 1966 until 1983, forged a strong friendship with Anna Freud and introduced his Yale colleagues to her.

The Anna Freud Centre, which was established during World War II as the Hampstead War Nurseries to treat traumatized children, had become one of the leading centers for the treatment and study of children with a range of serious developmental and psychological disorders. The Centre’s collaborations with Yale involved professors at the medical and law schools as well as colleagues in the community and on the clinical faculty. The ties between these two institutions continued with the leadership of Donald J. Cohen, M.D. ’66, who led the Child Study Center from 1983 until his death in 2001 and who, like Solnit, served on the Centre’s board of trustees.

Last July, the Centre appointed a new directorial team that includes, in addition to Mayes, Peter Fonagy, PH.D., and Mary Target, PH.D. Fonagy is the Freud Memorial Professor of Psychoanalysis and Director of the Sub-Department of Clinical Health Psychology at University College London. Target is a senior lecturer in psychoanalysis, also at University College London.

—John Curtis



A symposium in December at the Child Study Center brought together an international group of psychologists and psychiatrists.

TERRY DAGRADI (2)

An 1810 issue of the *Connecticut Mirror* announces the establishment of the Medical Institution of Yale College.

Newspaper heralds a new day in medical education—almost two centuries ago

Stop at medical grand rounds on any given Thursday morning and you're likely to encounter Samuel D. Kushlan, M.D. '35, HS '37, a retired gastroenterologist who has served on the faculty for 65 years and who turned 92 in February. Kushlan graduated from Yale College in 1932 and from the School of Medicine three years later, and his view of the school's history is a long one.

Kushlan's appreciation of the medical school's earliest days recently grew larger, however, when he was given a copy of a 19th-century newspaper documenting the school's establishment by an act of the Connecticut legislature. The slightly yellowed but well-preserved copy of the *Connecticut Mirror*, from November 5, 1810, includes the text of the act creating the Medical Institution of Yale College. The new school was the joint responsibility of Yale College and the Connecticut Medical Society, which today has its headquarters on St. Ronan Street in New Haven.

Yale's first medical students could expect to draw on the expertise of an initial faculty of four and core facilities consisting of "a Cabinet of anatomical preparations," "a collection of specimens, in the *Materia Medica*" and a botanical garden to be planted "as soon as the funds of the college can afford such establishment." Medical students who had finished college were required to study medicine for two years before entering the profession; those who hadn't would spend three years in class. In addition to attending lectures,

the students were expected to apprentice under a local physician or surgeon in good standing.

Kushlan came upon the newspaper through the good graces of Richard Lodish, principal of the lower school at Sidwell Friends in Washington, D.C., where Kushlan's granddaughter chairs the school's parents' organization. A collector of education memorabilia, Lodish thought of Kushlan when he saw the copy of the *Mirror* advertised on the Internet. Lodish has another New Haven connection: his daughter, Maya B. Lodish, M.D. '03, received her medical degree from Yale last May and is now a resident in pediatrics at Johns Hopkins.

While some early features of academic medicine remain unchanged (the act describes in detail the responsibilities of various committees, for example), recent graduates will be amused and possibly dismayed by one provision of the 1810 legislation noted below its description of the curriculum: "The price of the ticket for the whole of the above courses of lectures shall be fifty dollars," the act stated. But students had other expenses to take into account as well. Before passing their exams, they were required to pay \$10 to the treasurer of the medical society, \$4 to each of their examiners and \$8 to the president of the university. Full freight is likely to be a great deal more when the medical school marks its 200th anniversary six years from now.

—Michael Fitzsouza

PUBLIC ACTS, Of October Session, 1810.

An Act in addition to and alteration of an Act, entitled "An Act to incorporate the Medical Society."

§ 1. **B**E it enacted by the Governor, and Council, and House of Representatives, in General Court assembled, That the President and Fellows of the Medical Society be empowered, to unite with the President and Fellows of Yale-College, for the purpose of forming a Medical Seminary, to be styled The Medical Institution of Yale-College; agreeably to the following articles, agreed upon by and between the committee of the corporation of Yale-College, and the Medical Society of the State of Connecticut; as follows, viz.

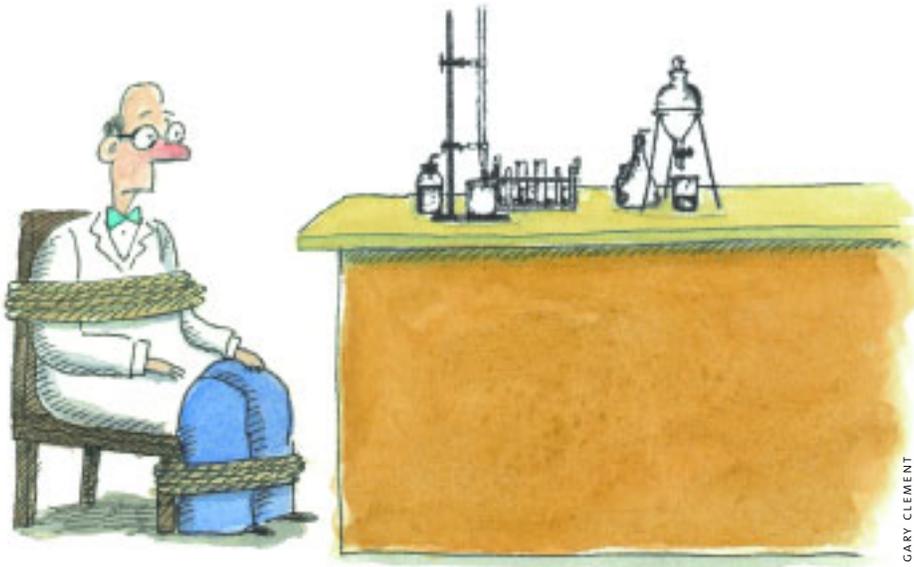
ART. 1. That there shall be a medical institution established in Yale-College, to be known and acknowledged by the name of The Medical Institution of Yale-College.

2. That said institution, to include a complete circle of medical science, consist of four Professors. First, of Chemistry and Pharmacy; Second, of the theory and practice of medicine; Third, of Anatomy, Surgery, and Midwifery; Fourth, of *Materia Medica*, and Botany. And that there shall be a joint committee of an equal number of persons, appointed by the convention of the Medical Society and corporation of Yale-College, who will make a nomination; from which nomination, the aforesaid Professors shall be chosen by the corporation.

3. That a Cabinet of anatomical preparations, including all things usually found in collections of this nature, be provided as speedily as the college funds will allow.

4. That there be a collection of specimens, in the *Materia Medica*: And that a botanical garden be established, as soon as the funds of the college can afford such establishment.

5. That every medical student be required to attend to the study of physic, or surgery, with some medical or surgical professor, or practitioner, who is in respectable standing, for two years; provided he shall have been graduated at some college; otherwise to study three years; and to have arrived to the age of twenty-one years. And that every medical student, who shall commence the study of physic, or surgery, after the foregoing articles shall be complied with, and lectures commenced, upon the several branches abovementioned, shall at-



GARY CLEMENT

Limits on stem cell research may preclude development of key therapies, panelists say

Nobody knows whether stem cells, the body's so-called "master cells" that can differentiate into other cells, will ultimately be useful for repairing diseased or damaged tissue. Current knowledge about possible therapeutic uses remains so limited, according to speakers on a panel on potential applications of the technology, that commercial development remains a distant hope in most cases. And panelists warned that medical applications may never occur because of current restrictions on research involving human embryonic stem cells.

According to Marc D. Beer, chief executive officer of ViaCell, a Boston-based company that banks stem cell-rich blood from umbilical cords for study and possible therapeutic use, "Stem cells have the potential to cure." But because of federal limits on the use of human embryonic stem cells, he said, "research is being curtailed. I'm watching basic research leave this country."

Beer was one of the panelists taking part in the third annual Yale and New Haven Biotechnology Reception in October. He pointed to recent successes in experimental clinical trials in which insulin-producing islet stem cells from donor pancreases have completely cured type 1 diabetes in some patients. "Lack of cells," said Beer, "is the biggest problem" for wider application of the transplant procedure.

Panel moderator Erin Lavik, sc.d., assistant professor of biomedical engineering, studies the use of stem cells for repairing damaged spinal cords. She said government restrictions, coupled with a possessiveness on the part of those who developed a few approved stem cell lines, are hampering research despite the fact that "we do not know the potential of these cells."

"When you don't know," said fellow panelist Earl M. Collier Jr., executive vice president of Genzyme Corp., "that's not the time to legislate."

—Marc Wortman

For undergrads, mentor program offers a glimpse of a physician's life

Five times during the fall semester, Shannon Gulliver, a Yale College senior majoring in microbiology, traveled from central campus to the medical school to observe Ali K. Abu-Alfa, M.D., as he tended to his patients. And her role at times went beyond mere observation. After palpating for edema on a dialysis patient's ankle, for example, he turned to Gulliver and asked: "What is the significance of this finding?"

The pairing of Gulliver and Abu-Alfa, an associate professor of medicine and director of the Peritoneal Dialysis Program, came as part of a new program, Yale Medical Professions Outreach (YMPO), designed to introduce undergraduates to the world of medicine. "I've always been very interested in science, but I didn't know much about patient relations," said Gulliver. "I was lucky enough to get a doctor who could talk about what aspects are fun, what aspects are harder, lifestyle sacrifices you have to make, time commitment and emotional commitment. I asked him very direct questions, and he was really into explaining."

YMPO was launched by students in January 2003 to create opportunities for undergraduates to observe physicians in their daily activities. "It's absolutely one of the most important things we can do for undergraduate students," said neurosurgeon Dennis D. Spencer, M.D., Hs '77, the medical school's interim dean and a YMPO participant. For years as a Yale College freshman advisor, Spencer invited his advisees to observe his interactions with patients, but it was always "hit-or-miss" for other undergraduates seeking physician contact, he said.

Yale seniors Steven Hsu and Jason Choi started YMPO to fill what they saw as a lack of premed preparation for undergraduates. "Yale has so many programs for students but nothing like

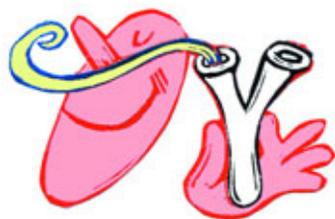
this,” said Hsu, who contacted Undergraduate Career Services and the medical school for guidance. A previous attempt at such a program ended when the founding students graduated. YMPO’s new leadership includes students from all classes to ensure continuity and growth. YMPO also started a lecture series, and in September added a Big Sibling/Little Sibling program that matches undergraduates with medical students. YMPO students must fill out an application and write an essay, and those selected are trained to comply with federal HIPAA regulations on patient confidentiality. Each student-physician pair sets its own meeting times for the semester. Sixty physicians are signed up, and last fall 70 students participated.

“I was immediately attracted to the program,” said Abu-Alfa. “Undergraduates are a body of students we don’t usually get to interact with. If you’re in love with what you do, to transmit that to a new generation is very exciting.”

—Mary Anne Chute Lynch



Yale College senior Shannon Gulliver shadowed nephrologist Ali Abu-Alfa over the course of the fall semester to learn about careers in medicine.



YALE RANKED AMONG BEST PLACES TO WORK

It’s often said that Yale is a highly collaborative institution, but how does one measure collegiality? *The Scientist* magazine did just that last fall in an international survey of 38,000 full-time U.S. faculty and researchers and found Yale among the best places to work in academia—third, actually, just behind Fox Chase Cancer Center in Philadelphia and Purdue University. Relationships with colleagues and the availability of resources were among the most important criteria for Yale respondents. “It is greatly rewarding to see our culture and investments acknowledged,” Provost Susan Hockfield, PH.D., said of the October 20 report, which can be viewed online at www.the-scientist.com.

—Michael Fitzsosa

et cetera ...

NEW PARTNERSHIP IN CHINA

On a recent trip to China, President Richard C. Levin and other university officers cemented a program of exchanges between Yale and Fudan University in Shanghai. The Fudan-Yale Center for Education Cooperation, one of several programs between Yale and Chinese universities, will build on educational exchanges that began in 1996.

The new center will promote exchanges among scholars in history, East Asian languages and literature, genetics, biology, law, medicine and management. The centerpiece of the agreement is the Fudan-Yale Biomedical Research Center. Tian Xu, PH.D. ’90, vice chair of genetics and special advisor to Levin on science and higher education in China, will direct both the education center and the biomedical center. Xu received his undergraduate degree at Fudan and his doctorate at Yale.

Xu said Yale has three goals—to help establish a world-class research center, to help Chinese educators reform their educational system and to promote understanding between the two countries.

—John Curtis

ONE PAPER, MANY IMPLICATIONS

A Yale geneticist is among the authors of an article deemed by *The Lancet* last winter to be the most important biomedical research paper of the previous year.

The authors of the article, “Genetic Structure of Human Populations,” published in *Science* in December 2002, used genotypes of more than 1,000 people from 52 populations around the world to study human population structure. “The paper quantifies the degree to which biomedical research findings based on one group of individuals may be applicable to individuals from other populations,” said co-author Kenneth K. Kidd, PH.D., Yale professor of genetics, psychiatry and biology. Kidd and colleagues in the United States, France and Russia identified six main genetic clusters and additional subclusters. They concluded that genetic risks of disease can be assessed with standard study designs if self-reported ethnic background is also considered.

—J.C.

At Liver Center, a vital organ gets its due

The nation's oldest liver research center sees a five-year renewal and expanding targets for therapies.

Poets and philosophers may rhapsodize about the human heart, but James L. Boyer, M.D., HS '67, says it's actually the liver that is the body's most fascinating organ.

"The ancients thought of the liver as the seat of the soul," says Boyer, director of the Liver Center at the School of Medicine and Ensign

Professor of Medicine. "Babylonians would consult a sheep's liver before going into battle, and even today, a Frenchman who is not feeling well is said to have *mal au foie*. European societies have much more respect for the liver than we do."

But at the Liver Center, the oldest research facility in the country devoted exclusively to liver research, this essential and complex organ gets its due. Roughly 40 scientists, all with independent funding totaling about \$15 million, study the liver.

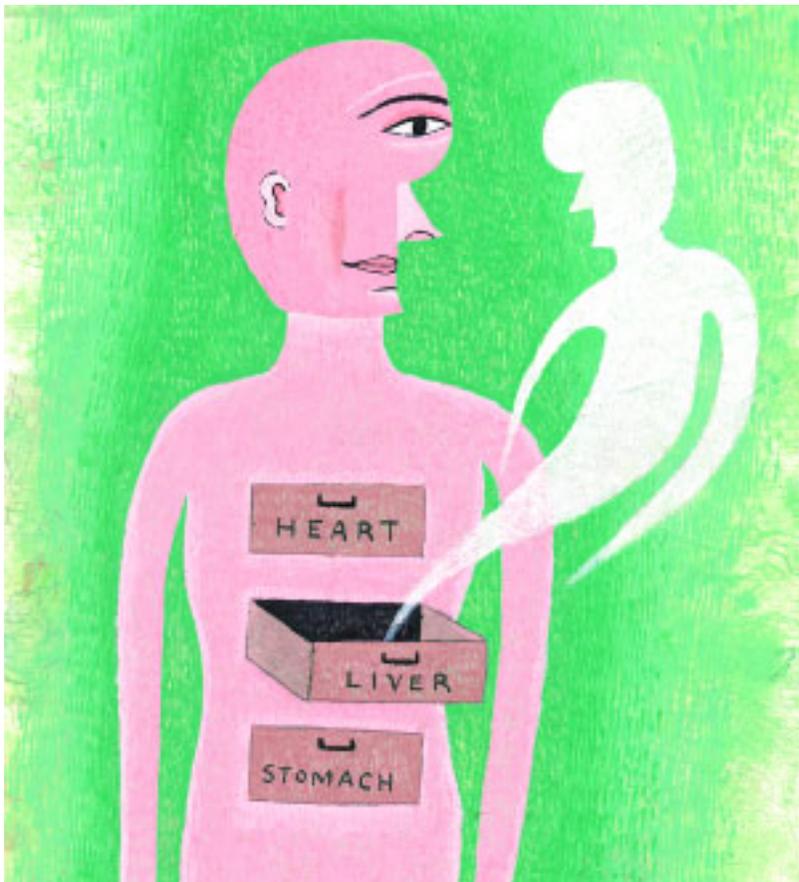
The value of the 20-year-old center was confirmed in December, when the

National Institutes of Health (NIH) renewed the center's funding for a fourth consecutive five-year term starting in September 2004. "We received the highest score in the history of the center," Boyer says of the NIH's evaluation. The center will receive \$3.75 million, with the university getting an additional 62 percent of that in indirect NIH support.

Hepatology has existed as a medical subspecialty for only 50 years, and as recently as 20 years ago there were still very few treatments for liver disorders. But Boyer says that is changing. He points out that hepatitis B and C and biliary cirrhosis can now be treated with medications. There is a vaccine for hepatitis A and B, and liver transplantation is now a viable option. In fact, Yale is expanding its transplant program with the recent arrival of David Cronin, M.D., a liver specialist, in the Department of Surgery.

But while some liver disorders are treatable, new challenges loom. The biggest, Boyer says, is fatty liver disease related to obesity. Gerald I. Shulman, M.D., PH.D., is a researcher in the Liver Center who has been studying liver diseases associated with insulin resistance. "Our work suggests that one of the earliest findings in type 2 diabetes is the presence of insulin resistance," Shulman says. "That starts to happen years before the development of diabetes."

Shulman's research has also found that insulin resistance occurs in the liver and the muscles, and that it is caused by a transport deficit triggered by the presence of fatty acids. "Fatty acids build up in the liver and lead to deficits in insulin signaling," he says.



MARLENA ZUBER



et cetera ...

OBESITY BIAS A PROBLEM FOR DOCTORS

Health professionals surveyed at an obesity conference in Quebec last year learned something surprising about themselves. The survey revealed a significant bias against overweight people among almost 400 physicians, researchers, pharmacologists and psychologists who treat and study obesity.

"The stigma of obesity is so strong that even those most knowledgeable about the condition infer that obese people have blameworthy behavioral characteristics that contribute to their problem, i.e., being lazy," said Marlene B. Schwartz, PH.D. '96, a research scientist in the Department of Psychology and lead researcher of the study published in September in *Obesity Research*. "Furthermore, these biases extend to core characteristics of intelligence and personal worth."

For the study 389 clinicians and researchers took the Implicit Association Test and filled out a questionnaire that assessed attitudes, personal experiences with obesity and demographic characteristics. The results were not all dispiriting, however. Those who work directly with obese patients showed less bias than those who do not.

—J.C.

SAME CHEMICAL, DIFFERENT REACTION

Drugs designed to improve memory consolidation in the elderly may also worsen working memory, according to a study by Yale researchers published in the journal *Neuron* in November.

The difference stems from the brain regions needed for different kinds of memory processing, according to Amy Arnsten, PH.D., associate professor and director of graduate studies in neurobiology. The hippocampus handles long-term memory, while the prefrontal cortex is responsible for working memory. The two brain areas, Arnsten found, respond to chemicals differently.

Medications in development to improve long-term memory often try to enhance the activity of protein kinase A (PKA), an enzyme inside of cells. Arnsten and her colleagues found that when this protein was activated in the prefrontal cortex it worsened working memory.

—J.C.

Shulman is now looking into the correlation between age and the onset of type 2 diabetes, even in adults who are not sedentary or overweight. "I'd say every third or fourth patient I see has adult-onset diabetes, which can have devastating complications," Shulman says. "We're working hard to sort it out." Many of these patients have fatty liver disease.

Other groundbreaking work being done by researchers at the Liver Center includes:

- Discovery of the gene responsible for isolated autosomal dominant polycystic liver disease and description of the clinical characteristics of this inherited disorder, by a group led by Stefan Somlo, M.D., FW '91.
- Fundamental discoveries made by a team led by Roberto J. Groszmann, M.D., at the VA Connecticut Health-care System in West Haven and William C. Sessa, PH.D., which have paved the way for therapies that will control the complications from portal hypertension in cirrhosis, such as intestinal bleeding.
- Demonstration that bone marrow cells are capable of migrating and establishing themselves in other tissues, such as the liver, by Diane S. Krause, M.D., PH.D. This pioneering work is central to the future of gene therapy for genetic liver disorders.

"When I started out, we were mainly diagnosticians. We couldn't cure many liver diseases," Boyer says. "The changes have been enormous. It's an exciting time to be working in this field."

—Jennifer Kaylin

Spike in blood pressure may make weight lifters vulnerable to aortic aneurysm

In a research letter published in *JAMA: The Journal of the American Medical Association* in December, a team of Yale researchers reported that some weight lifters may be at risk of rupturing the aorta's inner lining.

"We had seen a couple of patients in a row who had been weight lifting when this phenomenon occurred," said John A. Elefteriades, M.D. '76, HS '81, FW '83, chief of cardiothoracic surgery. Looking through his research projects, he found other cases. "I noticed that two or three of them were young people who otherwise wouldn't have been expected to have an aortic dissection and were lifting weights at the time."

They found that systolic pressure during heavy weight lifting can rise from a normal reading of 120 to highs of 280 and even 300. "If your aorta is weak due to your genetics and if it is mildly enlarged, weight lifting might be what puts you over the brink," Elefteriades said.

The danger of a potentially fatal aortic dissection, which splits the artery in two, results from a confluence of events, starting with that genetic predisposition.

Elefteriades is working to pinpoint the genetic links in association with Celera Genomics, the company involved in the mapping of the human genome.

Those at risk include people with aneurysms, connective-tissue diseases and hypertension, as well as people with a family history of aneurysms or dissections and those above age 40.

—John Curtis

A partnership that aids cancer's migration

When *Ras* teams up with cell polarity genes, mutations are found to produce metastatic tumors.

In the world of cancer-causing genes, *Ras* is a celebrity. Mutated versions of this gene appear in more than half of all human cancers, including metastatic cancers, in which cells from a primary tumor disperse to other organs or systems of the body and there give rise to new tumors. Clearly, *Ras* is a culprit in many terminal cases. But since a large number of *Ras*-based tumors are benign and never spread beyond their original site, it was thought that the oncogenic *Ras* triggers only tumorigenesis. Now, research demonstrates that *Ras* also contributes to metastasis and it collaborates with a partner to do so. Tian Xu, PH.D. '90, professor and vice chair of the Department of Genetics and an associate investigator for the Howard

Hughes Medical Institute (HHMI), has identified five genes that interact with *Ras* to cause metastasis.

Each of these “cell polarity genes” normally fills an important role in maintaining the orientation of the cell with regard to the inside or the outer surface of the body. The normal version of *Ras*, meanwhile, transmits signals that aid in development by controlling the rate at which various cells reproduce and differentiate. Although neither a mutation in a cell polarity gene nor a mutation in *Ras* leads to malignancy on its own, Xu and graduate student Raymond Pagliarini have shown in an animal model that when tumor cells have both mutations, they invariably produce metastatic tumors.

The scientists arrived at these findings by creating a genetic screen in *Drosophila melanogaster*, the fruit fly. If *Drosophila* seems at first to be an unsuitable model for humans, it is only because our outer forms look so different. Inside we have a great deal in

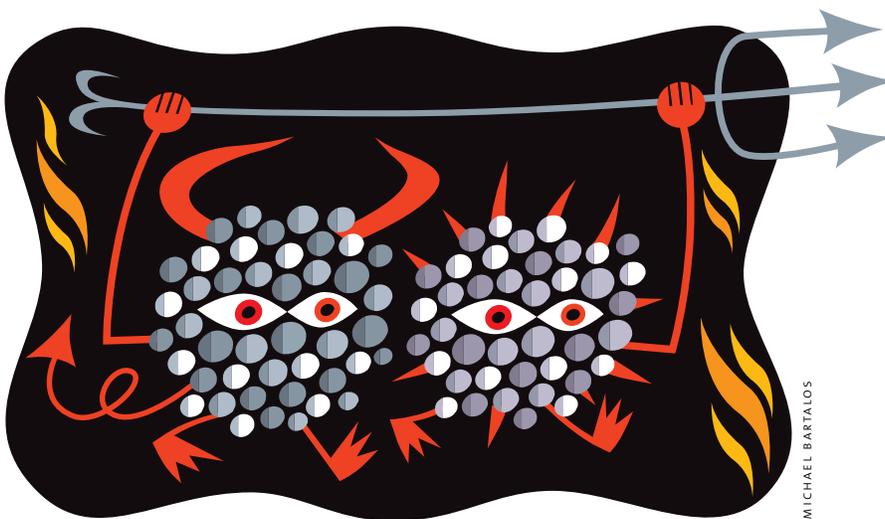
common: for instance, 70 percent of the disease-causing genes in humans also appear in the fruit fly. Xu and Pagliarini first used fruit flies with mutant *Ras* genes to create noninvasive tumors in developing larvae, then added other mutations to see whether the tumors become metastatic. Although only a handful of these combinations produced the results they were looking for, Xu and Pagliarini's observations are likely to spur the development of new drugs for cancer treatment, targeting genes that collaborate with *Ras* to deadly effect.

As for *Ras* itself, this gene has been in the sights of pharmaceutical companies for some time now, and Xu points out that it still represents a good target for anti-cancer drugs. “Inactivating the tumor-producing effect of mutant *Ras* genes,” he says, “will likely be simpler than re-creating the tumor-suppressing effect of genes that are no longer normal, but mutated.”

As Xu sees it, “cancer is generally a late-stage disease—but in most of human history, longevity was much lower than it is now. People didn't live long enough to get cancer.” What then was the original function of these genes? “We believe they are normally involved in regulating development, especially the size of cells and tissues, and ultimately the size of whole animals,” Xu says.

The most exciting aspect of Xu's work on the metastatic partners of *Ras* is undoubtedly its clinical potential, but in Xu's eyes this series of experiments offers another far-reaching benefit as well. “This work really showed the power of model organisms like fruit flies, because we can use them to do a lot of experiments that would not be possible in humans,” he says. It was this painstaking, gene-by-gene screening that allowed researchers to find the specific gene interactions that lead to metastasis, and thus to identify the drug targets that look so promising today.

—Sandra J. Ackerman



et cetera ...

GENE MUTATION LINKED TO OCD

A mutated gene's link to a rare form of obsessive compulsive disorder (OCD) is the strongest proof yet that neuropsychiatric disease can result from a malformed neuronal protein.

In studies published last October and August in *Molecular Psychiatry* and *Molecular Pharmacology*, researchers at Yale and the National Institute of Mental Health found that a rare form of OCD is associated with a mutation in the serotonin transporter gene that disrupts the normal regulation of transport.

"There are not a lot of established connections between genes and behavior," said Gary Rudnick, Ph.D., professor of pharmacology, who conducted the research with Fusun Kilic, Ph.D., of the University of Arkansas for Medical Sciences. "Our finding focuses on the role of the serotonin transporter in mood and behavior and ties it to a specific behavioral disorder."

The researchers found in two unrelated families a gene mutation that increases uptake of serotonin by the transporter. Further study could lead to a better understanding of how OCD develops and how medications might affect the serotonin transporter.

—John Curtis

HONORS FOR IMMUNOLOGIST

Scientists from around the world gathered in November to honor the late Richard K. Gershon, M.D. '59, 20 years after his death and 30 years after his discovery of suppressor T cells.

Gershon started his career as a pathologist and switched his focus to immunology when he began working on a tumor model in hamsters. His discovery was initially greeted with skepticism, but suppressor T cells, which reduce the immune response of other cells to antigens, are now seen as vitally important in a variety of diseases. In recognition of his work, Gershon was elected to the National Academy of Sciences in 1980.

A lecture has been held in his honor each year since his untimely death in 1983, but this year the Section of Immunobiology and his family noted his passing with a symposium that featured leaders in suppressor T cell research.

—J.C.

Divining the scent of a human: for mosquito, it's a molecular event

To most people perspiration ranks low on lists of attractive features, but one creature finds the smell of human sweat irresistible: the female of *Anopheles gambiae*, commonly known as the mosquito. Just what makes our perspiration so alluring to this ruthless predator is a question that intrigues not only the companies that make insect repellents and the people who use them, but most of all the epidemiologists trying to reduce the toll of mosquito-borne diseases.

Now scientific research is beginning to reveal an answer. John R. Carlson, Ph.D., professor of molecular, cellular and developmental biology, Elissa Hallem, a graduate student in the Interdepartmental Neuroscience Program, and colleagues have developed a transgenic technique that allows them to identify the functions of specific odor receptors in the mosquito antenna. Their paper, published in the January 15 issue of *Nature*, describes how the researchers pinpointed the receptor gene, *AgOr1*, and the compound to which this receptor responds, the odorous molecule 4-methylphenol.

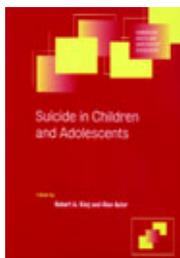
The scientists used a "knockout" fruit fly lacking one of its odor-receptor genes. They substituted the mosquito gene *AgOr1* and then measured the animal's response to various odors; the only molecule to produce a strong response was 4-methylphenol. A similar gene, *AgOr2*, used as a control, showed no such response. This observation, together with previous findings that *AgOr1* is present only in female

mosquitoes and that the expression of this gene tends to diminish after the mosquito has had a blood meal, suggests that the *AgOr1* receptor plays an important role in the mosquito's hunting and feeding behavior.

According to Carlson, this work puts researchers "on the right track" toward developing a truly effective mosquito repellent. "If we can find each of the odor receptors and identify the specific compounds they're responding to, the next step would be to come up with inhibitor or blocker compounds, which would bind to the receptors but not activate them," he explains. The mosquito would thus be unable to perceive the odors that normally lead it to a human banquet. Large numbers of people might be protected from bites, or from life-threatening infections. (The mosquito-borne disease malaria kills an estimated one million people each year, most of them children.)

The research on odor receptors may also have a direct application in insect control: the odors most attractive to mosquitoes could be used to lure the insects away from human populations and into traps where they could be destroyed. In principle, says Carlson, the same techniques might even be used against crop pests. But he cautions that "the system we have created, a system that can identify odor-receptor genes, has not yet been applied in other insects." With the work on mosquitoes yielding such promising results, progress on dealing with other insects is probably not far behind.

—S.J.A.



Suicide in Children and Adolescents

edited by Robert A. King, M.D., professor of psychiatry and a member of the Child Study Center, and Alan Apter

Cambridge University Press (Cambridge, United Kingdom) 2003; 334 pages

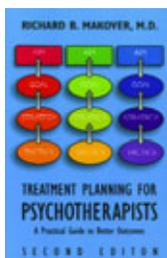
Experts from psychiatry, epidemiology, neurobiology, genetics and psychotherapy bring together the most recent findings in their fields to address important questions about suicide. How can these deaths be prevented? Can they be anticipated? Are there perceptible patterns? What role do families and gender play? What are the treatments for and outcomes of suicide attempters?

Treatment Planning for Psychotherapists: A Practical Guide to Better Outcomes, 2nd ed.

by Richard B. Makover, M.D., lecturer in psychiatry

American Psychiatric Publishing (Washington) 2004; 208 pages

This handbook offers a clear, concise explanation and clinical-case examples of practical treatment plans from initial assessment, through diagnosis and formulation, to the critical decisions about objectives, methodology and technique.



Dementia: A Practical Guide

by Marc E. Agronin, M.D. '91

Lippincott Williams & Wilkins (Philadelphia) 2003; 272 pages

This latest addition to the *Practical Guides in Psychiatry* series is a pocket manual written for everyone from medical students to fellows to psychiatrists, neurologists and internists in practice who want a concise guide to dementia at their fingertips.

A Practical Approach to Transesophageal Echocardiography

by Bessie L. Marquis; edited by Scott T. Reeves and Albert C. Perrino Jr., M.D., HS '87, associate professor of anesthesiology

Lippincott Williams & Wilkins (Philadelphia) 2003; 352 pages

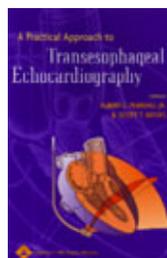
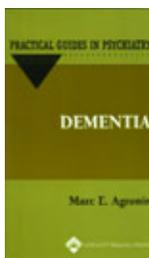
This text offers a concise guide to the current practice of transesophageal echocardiography and includes discussions on its uses in surgical procedures and on data derived from Doppler studies.

Clinical Neuroanatomy, 25th ed.

by Stephen G. Waxman, M.D., PH.D., chair and professor of neurology and professor of pharmacology and neurobiology

McGraw-Hill/Appleton & Lange (New York) 2002; 400 pages

This text links basic concepts in neuroanatomy with clinical correlations. The new edition reflects the state-of-the-art in the pathophysiology, diagnosis and treatment of neurological disorders and discusses the latest advances in molecular and cellular biology in the context of neuroanatomy.



Ellenberg and Rifkin's Diabetes Mellitus, 6th ed.

by Daniel Porte Jr., Robert S. Sherwin, M.D., C.N.H. Long Professor of Medicine, and Alain Baron

McGraw-Hill Professional (New York) 2002; 1,047 pages

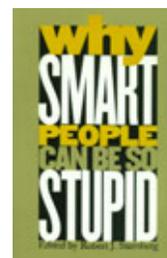
This text is a comprehensive reference on diabetes mellitus, covering basic biochemistry, physiology and pathogenesis, as well as clinical diagnosis and treatment. The sixth edition includes five new chapters, plus new material on the genetic basis of the disease, new hypoglycemic drugs, mechanisms of hormone action and regulation of hormone secretion.

Child and Adolescent Psychiatric Clinics of North America: Psychological Aspects of Chronic Disease

by Lawrence A. Vitulano, PH.D., and Melvin Lewis, M.B.B.S., F.R.C.Psych., HS '59

W.B. Saunders Co. (New York) 2003; 598 pages

Chronic illness in childhood presents many challenges for the child and adolescent mental health clinician. This book examines several major chronic illnesses in depth to provide a better understanding of the physical demands, medical treatment requirements, social limitations and general prognosis for the child.



Why Smart People Can Be So Stupid

edited by Robert J. Sternberg, PH.D., IBM Professor of Psychology and Education

Yale University Press (New Haven) 2003; 272 pages

This book investigates the psychological basis for stupidity in everyday life. Experts shed light on the nature and theory of stupidity, whether stupidity is measurable, how people can avoid stupidity and its consequences and more.

The Perfect Fit Diet: Combine What Science Knows About Weight Loss With What You Know About Yourself

by Lisa Sanders, M.D. '97, HS '00, clinical instructor in medicine

Rodale Press (New York) 2004; 358 pages

Building on her research analyzing more than 700 weight-loss programs, Sanders has "uncovered a fundamental truth about dieting," according to the publisher, that "sustainable weight loss is only possible on a diet that fits [one's] food preferences, satiety signals, lifestyle and medical profile." Sanders, who also writes the monthly "Diagnosis" column in *The New York Times Magazine*, offers a plan for tailoring eating habits and activities to lose weight and keep it off.

The descriptions above are based on information from the publishers.

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



MICHAEL MARSLAND

BILL CLINTON

In global cooperation “... every human being counts”

Long-term stability for the United States depends on fostering international cooperation, not as a last resort but as a priority, former President Bill Clinton told an enthusiastic crowd of more than 2,000 at Woolsey Hall last fall. In an explicit critique of the Bush Administration’s foreign policy, Clinton said Americans should “cooperate whenever we can and act alone only when we have to, and not the other way around.”

A multilateral approach is vital to combat AIDS and other diseases: “You cannot zap a microbe with a missile,” said Clinton, who was in New Haven for his 30th law school reunion in October. And by reaching out to help struggling nations, the United States also serves its own interests. “This is not rocket science, but every time we do it, we build a world with more friends and fewer terrorists.”

The foundation of global cooperation, Clinton said, is the idea that every human being counts. And that means leaving ideology aside, he said. “Because once you believe you have the absolute truth, then it’s not possible for everyone to count. ...”

—Cathy Shufro



MICHAEL FITZSOUSA

ANDREW GILMAN

Encouraging physicians to speak “the appropriate language”

Media consultant Andrew Gilman once coached a NASA engineer who was part of the effort to repair the Hubble Space Telescope. Preparing him for a television interview, Gilman winced at the engineer’s description of the evening’s mission: “At 23:50, we’ll effect an EVA and recalibrate the module.”

Did that mean, Gilman asked, that an astronaut would take a space walk at 10 minutes to midnight and adjust the telescope by a few millimeters?

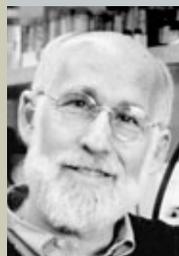
“Yes,” the engineer said.

“Jheesh,” replied Gilman. “No wonder you can’t get money from Congress!”

Speaking at psychiatry grand rounds in October, Gilman advised faculty members who speak to the press to keep their messages simple and focused. Three points repeated three times during an interview communicate more than nine points made once, he said. It also pays to find out a little about the reporter and the story angle before launching into an interview, and to keep the school’s media relations staff in the loop.

Gilman also dismissed the notion that science is too complex to be conveyed to the public. Citing the example of the NASA engineer, he urged his audience to use plain English. “It’s not dumbing down,” he said. “It’s speaking the appropriate language.”

—Michael Fitzsosa



MICHAEL RONNEN SAFDIE

JEROME GROOPMAN

Keeping hope alive for the seriously ill

As a physician caring for seriously ill AIDS and cancer patients, Jerome E. Groopman, M.D., has learned that doctors need to temper their prognoses with humility, regardless of how bleak the patient’s outlook may appear. “We should not sit like a judge and hand down a death sentence,” he said during a visit to Yale in November. “Never write someone off a priori.”

Delivering the Iris Fischer Lecture, the bestselling author, Harvard Medical School professor and chief of experimental medicine at Boston’s Beth Israel Deaconess Medical Center recounted some of the stories and themes from his recently published book, *The Anatomy of Hope: How People Prevail in the Face of Illness*. In the context of illness, he said, hope and science are often in conflict. “There’s a tension in how to be truthful to patients and ourselves and not take away hope,” he said. “We have to be careful about slamming the door on hope.”

His patients’ efforts to derive meaning from their illness, he said, offered a lesson about hope. “Hope arrives,” he said, “when you believe you have real choices to make, when you believe the future can be different than the present.”

—Marc Wortman



ANDREW FOSTER/JHS/PH

NGA LIEN TRAN

Examining how a chemical enters the food supply

Health and safety experts are trying to solve a fast-food mystery: why does a probable human carcinogen appear in such foods as French fries and potato chips, and how much of a health risk does it pose? Nga Lien Tran, DR.PH., M.P.H. ’85, senior managing scientist at Exponent and adjunct assistant professor at the Bloomberg School of Public Health at Johns Hopkins University, discussed the puzzle at the November 2003 Interdisciplinary Risk Assessment Forum sponsored by the Institution for Social and Policy Studies at the Peabody Museum. According to Tran, studies conducted by the Swedish National Food Administration and researchers from Stockholm University confirmed in April 2002 that unexpectedly high levels of acrylamide—a chemical used in making cosmetics, plastics and adhesives—were found in some starchy foods after frying or baking at high temperatures. The darker and crispier the food, the more acrylamide was present.

The good news, Tran said, is that neurotoxicity resulting from acrylamide exposure—which has been known to kill fish and paralyze cows—doesn’t appear to be a concern. However, people who consume a lot of these foods may increase their lifelong cancer risk by an order of one in a thousand. “We’ve let the public know, and we’re continuing to monitor and measure,” she said. “At this point that’s all we can do.”

—Jennifer Kaylin

Marie Curie at Yale

Despite her scientific eminence, a warm welcome and an honorary degree, the Nobel laureate endured a few slights during her 1921 visit to New Haven.

By John Curtis

MELONEY-CURIE PAPERS, RARE BOOK AND MANUSCRIPT LIBRARY, COLUMBIA UNIVERSITY LIBRARIES



Although Marie Curie tended to shy away from journalists, she hit it off with Marie (Missy) Mattingley Meloney, left, editor of a women's magazine called *The Delineator*. Meloney organized Curie's 1921 American tour and promised to raise \$100,000 to buy a gram of radium. Curie's daughters Irène and Eve, right, joined her on the tour.

When Marie Curie came to Yale in 1921 to receive an honorary degree, opinions among the faculty were decidedly mixed. Although six women had already received honorary degrees from Yale, she was the first to receive an honorary SC.D. Her nomination had come not from the Faculty of Arts and Sciences, but from physicians at the School of Medicine, who had corresponded with the Nobel laureate about the uses of X-rays and radium. Some chemists and physicists on the faculty thought the award was a mistake.

Among them was Bertram B. Boltwood, PH.D., a Yale professor and a leading radiochemist, who felt that the physicians' recommendation was a bit hasty. "When he learned Curie wished to visit him, he told the Yale administration he had no desire to have the honor thrust upon him," said Daniel J. Kevles, PH.D., the Stanley Woodward Professor of History. "He considered it the duty of the institution to entertain her."

Kevles was one of three panelists to discuss the "Intellectual Journeys of Marie Curie" at a three-day symposium in November to celebrate the centennial of Curie's first Nobel Prize and to honor women in science. An exhibit at the Cushing/Whitney Historical Library also examined Curie's life and legacy.

Curie seems to have been destined to lead an unconventional life. She was born into a Polish family that included a grandfather who harbored the revolutionary notion that the children of peasants and nobles should go to school together. Her father was demoted from his job as a school headmaster for consorting with "radicals." Marie Curie herself was illegally taught the Polish language, history and literature as a child and got around the ban on higher education for women in occupied Poland by attending an illegal, clandestine university. She later courted exile to Siberia for the crime of teaching peasant children to read and write.

Years later in Paris she would meet and marry an equally unconventional

man. Pierre Curie was an outsider to the French scientific establishment who had not attended the right schools. In 1903, when he and a colleague were under consideration for a Nobel Prize, his sense of fairness demanded that a third collaborator in their studies of radiation also be included. So it was that Marie Curie received her first Nobel Prize, in physics. Her second, in chemistry for the discovery of radium and polonium, came in 1911, several years after her husband died in an accident.

Their strongly held beliefs would not allow the Curies to profit from their discoveries. “They made a deliberate decision not to patent the process for purifying radium, believing it belonged to the public,” said Sara Rockwell, PH.D., professor of therapeutic radiology and director of the office of scientific affairs at the medical school, who also spoke at the symposium.

The United States that Curie visited in 1921 offered a bleak landscape for women in science. They were paid less than men and promoted more slowly. Most found jobs in women’s colleges that lacked the resources of larger schools. “Coeds could celebrate Marie Curie, but in the 1920s, few wanted to emulate her,” Kevles said.

Her tour culminated in a visit to the White House, where President Harding presented her with a gift of a gram of radium.

Yet even as a Nobel laureate and guest at the White House, Curie was not immune to discrimination on her American tour. The physics department at Harvard blocked an honorary degree for her, and rather than address the question of whether to admit women, the National Academy of Sciences declined to accept her as a member. And there was her reception at Yale.

Despite Boltwood’s antipathy toward her, the citation that accompanied Curie’s honorary Yale degree was warm and effusive. “It is superfluous to mention her discoveries in science and now she has discovered America. She has often encountered dangers in scientific experiments, but nothing so dangerous as American Hospitality; it is to be hoped that she will not be a Woman Killed with Kindness. She is unique. There is only one thing rarer than genius, and that is radium. She illustrates the combination of both.”

And eventually, Curie won over even Boltwood.

“In the end,” Kevles said, “Boltwood did receive Curie in his laboratory and was in fact impressed by her keenness in scientific matters and also her personal amiability.”

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

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1921 THE YALE ALUMNI WEEKLY 1101



MADAME CURIE RECEIVES HER YALE DOCTORATE OF SCIENCE.

Although six women had previously received honorary degrees from Yale, at the 1921 Commencement Curie became the first to receive an S.C.D.



Bertram Boltwood, a leading radiochemist, initially balked at a request to receive Curie in his laboratory at Yale. When Curie did visit him, he was impressed by her keenness in scientific matters.



Jenny Blair likens her Harkness apartment's quirks to those of an old friend. The bathroom door sticks, layers of paint cover everything and her oven overheats by 100 degrees. But, she says, "these are all part of the charm of the place."

By Jenny Blair
Photographs by Terry Dagradi



“That college feeling”

What student in her right mind would choose to live in a dorm for all four years of medical school? Ask Jenny Blair, who enjoyed a gym in the basement, a piano in the Harkness ballroom and snowball fights right outside the door.



Midtown, Hyde Park, Brookline. Match Day is upon us, and I am looking for a neighborhood in the cities whose hospitals I've applied to. Soon I will be looking for an apartment. Strange though it sounds, it will be hard to improve upon the one I have on the medical school campus.

Our class moved into Harkness Dormitory in August 2000, after renovations had polished it back to new. The doors swung smoothly. The floors were so clean that it felt like sacrilege the first time your bare feet felt the crunch of dirt on them. The low-pitched, constant whoosh of building ventilators coming from the courtyard—or the ripping decibels of motorcycles on the Frontage Road side—became our lullabies. We had sinks in our rooms, clean tiled bathrooms down the hall and windows generous enough to help the building shed its old nickname (“You don't live in Darkness Hall, do you?” asked a smart aleck I met through an online dating service).

Though I'd known the freedom of apartment life during my years at Yale College, I initially opted for the dormitory for social reasons. Ask almost anyone who chooses Harkness and they'll say the same thing, though they'll mention the location and the in-house cafeteria and the relief of not needing to look for an apartment in a strange city. New Haven was no novelty to me; I could have picked out a porch-and-yard in the Grad Ghetto in the East Rock neighborhood or on Prospect Street with

English and physics students as neighbors. But I wanted to start medical school with my very own class. So I wedged belongings from the three-bedroom shared apartment I'd occupied during a post-college year into a tiny room beside the elevator, on the eighth floor. It was small, but near everybody else, including students from the other health schools, and you couldn't beat the commute—though that didn't keep us from trotting down Cedar Street late for morning lectures, slinking into the back of Hope 110 with coffee in hand.

A room with a view

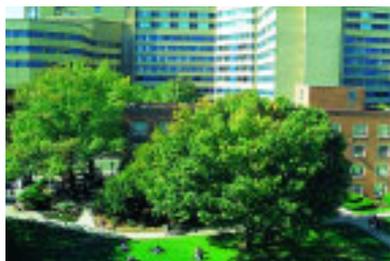
I nested quickly, decorating the door with photos from magazines and the obligatory message board, and coming to relish the view from my window: food-cart picnickers on the grass, day-care kids playing and always the stately Sterling Hall of Medicine, with odd windows lit at night. The eighth floor was all-female, and peaceful. The happenin' floor was the ninth. It was there that we threw our parties; people strung black bags over the ceiling lights, and someone DJ'd with his own equipment and we all felt like college freshmen again, only much cooler. These days, first-year students use the ninth floor's kitchen to get together for a weekly dinner they cook themselves.

But no one, it seems, wants that college feeling for long. My classmates, almost to a person, stopped living on the med school campus after their first year. The many perks—Tuesday-night *Queer Eye for the Straight Guy* (or, when we were first-years, *Temptation Island*), instant access to food carts, laundry machines, Ethernet, even the lack of any commute to Yale-New Haven Hospital (which can mean an extra half-hour of sleep during tough rotations)—don't seem to overcome the stigma of a dormitory. Most people moved into high-rises two blocks away, or up to the Science Hill neighborhood, where they walk their dogs and jog past lawns, bushes and postdocs out with spouse and stroller. After four years, though, I'm one of the few die-hards still living here, though I switched to the apartment side of Harkness during second year. (Harkness Apartments is Harkness Dormitory's endearingly scruffy neighbor.

Whether for reasons of convenience, aesthetics or sociability, Harkness has always lent my medical school experience something inimitable.

Living in an apartment overlooking Harkness Lawn keeps Blair connected to the school and classmates. “Friends walk by and wave for me to let them in, and I always know when impromptu snowball scrimmages are on.”

Edward S. Harkness Hall turns 50 in 2005; see *Archives* on page 48.



Positioned at right angles to the dormitory—the two buildings hug the courtyard—it is only four stories high, and its units are one-bedroom apartments instead of studio-style dorm rooms. Together they are Edward S. Harkness Hall.) Whether for reasons of convenience, aesthetics or sociability, Harkness has always lent my medical school experience something inimitable.

On the happenin' floor, communal meals

I wondered how other students felt about it. On a recent Sunday evening I revisited the ninth floor to check out the fabled communal meals. When I arrived, a dozen or so students were watching football on TV and eating a pepper-speckled Caesar salad from a big bowl. Two women hovered over great pots of chili on the stove. Empty cans and packages of guacamole littered the counter. A keg waited expectantly in a corner.

Eyeing the generous bowls of corn chips, I sat down beside a first-year named Brendan Jackson who, as it turned out, was a member of a mysterious sixth-floor Frat. “It’s very unofficial—Ru-Rah-Rigma,” he explained mysteriously. “There’s a fraternity on the sixth floor?” asked a classmate. (It’s an all-male floor.) “Yeah. Live on the sixth floor and you’re in.” Jackson is also the Harkness Dorm Liaison. He had recently been elected by his classmates, though he ran unopposed. His duties include presenting the dorm dwellers’ complaints to the Powers That Be. Complaints like what? “The water pressure!” he answered. “None of the TVs work except the one on the ninth floor,” put in a woman who was standing by. Maybe that’s how the ninth floor got so popular.

The home-cooked dinners began because the dining hall is closed on weekends. They were the brainchild of

first-years Caryn St. Clair and Misaki Kiguchi. When I first saw Misaki, words like “brisk” and “efficient” came to mind. As students slipped into the lounge, she swung between kitchen and tables as if on a hinge, handing off bowls of chili topped with blue corn chips, purple onions, guacamole, sour cream and shredded cheese to one eater after another. The room grew happy and noisy, and soon people were wading through the crowd to the keg and helping themselves. I stretched like a cat and enjoyed the atmosphere.

Tired of eating at Subway every weekend, Misaki convened a group of students willing to take turns catering for each other. She makes up the schedule and e-mails it to everyone involved. When people who aren’t part of the circuit show up to mooch, she publicly assigns them a night to cater for the group, trusting in the potential wrath of 40 hungry classmates to exert the necessary social pressure. Dishes served in weeks past have included chicken Marsala, pancakes and caramel apples. As I chatted with the diners, an arm reached into our midst and set down a big pan of

sliced blueberry cornbread. I took a piece, ate it, then took another. Though I was too afraid of being forced to cater for 40 people to sneak a bowl of chili, resistance to cornbread was futile.

Remembering what it was like trying to fit my complicated mess into one room, I asked the general assemblage if anyone had decorated really creatively. One of their number was pushed forward, protesting feebly. “You’ll see what can be done with a Harkness room,” they promised me. The student in question, willing but abashed, led me to his room and unlocked it.

This man had a gift. Red curtains, sleek pine bookshelves, delicate fabric lamps shaped like Platonic solids, a tidy futon, a patterned rug instead of the standard ratty Persian knockoff, a graceful easy chair. It was Urban Outfitters, it was Ikea, it was glorious. It even smelled good.

Yet even he is planning to leave, as is every current first-year I asked.

I stayed. I love living in Harkness. Friends walk by the window and wave for me to let them in, and I always know when impromptu snowball scimmages are on. The basement gym is too close for excuses. I can walk downstairs with a folder of music and practice the piano in the ballroom. In late evening I can slip across the lawn to the computer lab or library—the lack of psychological distance between work and home life doesn’t bother me, for some reason. Here on the apartment side, the dormitory gods even provide free furniture. My couch and easy chair began life as seating for interviewees in the Office of Student Affairs. Tacit neighborly trades go on all the time, as when a bookshelf or night table turns up in a hallway and a day later is eased, skittering, into someone else’s room.

I prefer the apartments for a few reasons. For one thing, I’m not an elevator person. As anyone who has watched me can tell you, I tend to stride purposefully toward my destination. Elevators interrupt the vector. The Harkness elevators were particularly irksome because they were often out of order. This happened so often that I learned to build it into my day, leaving extra time to get up and down the stairs on days when the building was competing for a single elevator. Living on the eighth floor, it was just barely worth it to wait rather than take the stairs, but I never learned patience. Apologetic signs appeared on the elevator doors over and over again, and soon we all knew where the first-floor stairwell door was. When I moved into Harkness Apartments, I chose a second-floor unit. Suddenly it was possible to run home from the hospital and pick up a forgotten stethoscope or heat up some lunch.

A decided advantage to the apartment side of Harkness, indeed, is the kitchenette. Though I’m no chef, it can be hard to transition back to a meal plan after having lived in an apartment. The dormitory’s common-room kitchens come complete with sink, stove, microwave and

freezer (“NOT A REFRIDGERATOR [sic],” a sign reminds us). But their public location creates a certain tension between the shared and the owned. Some people take their chances and leave things there. When I was a first-year, one student used to leave her carton of eggs out on a shelf. I doubt anyone stole an egg, but I remember slices gone missing from the loaves of bread I stored in the freezer. Annoyed, I piled breakfast fixings onto a cart every morning—pot, oatmeal, eggs, plate, fork, spatula—and wheeled it into the elevator to ride one floor up. Ding. But the dumpy little cart dampened any culinary ambitions I might have had after managing breakfast. Now that I have a kitchen of my own, I’ve upgraded to soups and stir-fries.

Like an old friend

It’s taken some practice, though. In contrast to the spanking-clean Harkness dorm rooms, the apartment side hasn’t been renovated. I like it that way; my apartment’s quirks are like an old friend’s. It’s the type of place where everything is covered with layers of paint—radiators, light switches, coat hooks. Every piece of furniture is an orphan. Several generations of curtain rods grace each window. The window in the bedroom is stuck slightly open year-round, while the bathroom door, if fully closed, traps guests inside (if I forget to warn them, I have to kick it open while they cower behind the sink). The oven reliably overshoots by 100 degrees, and the markings wore off the burner dials ages ago. But these are all part of the charm of the place, and I’ve mastered the workarounds. With vigilance and a thermometer, I can even wrest pie from the oven.

Do fourth-year medical students get “senioritis”? As part of final-semester lassitude, I spend a lot of time daydreaming about my next place, as well as reminiscing. I’ve lived in a lot of apartments. There was a New Haven summer sublet on Bishop Street, with hardwood floors that sloped and roaches so ubiquitous that I kept dishes buttoned into Tupperwares to keep them clean. There was a carpeted one in Ann Arbor, an easy walk from downtown, that smelled of the downstairs neighbor’s ferrets. At night a freight train hustled by, waking me, then soothing me back to sleep. There was a flat in Fort Lauderdale that huddled in a patch of downtown jungle. I remember wet heat, ants streaming across the windowsill to the spot of jelly on the counter, peacocks strolling outside. The year after graduating from Yale College, I lived in New Haven in a place memorable more for its roommates—a bread-baking astrophysicist, an Orthodox Jew who knew six languages and a geologist obsessed with bunnies and Renaissance Fairs—than for its physical plant. Then I was accepted to Yale Med. For four years, Harkness has welcomed me home, and I could hardly ask for better. **YM**

Fourth-year student Jenny Blair will begin a residency in emergency medicine this summer at University of Chicago Hospitals.

A bed at Ma Levin's, dinner at Nick's and nary an e-mail in sight.

It's been more than half a century since Arthur C. Crovatto, M.D. '54, HS '61, was a first-year Yale medical student living in Ma Levin's boarding house on Howard Avenue, but he can tick off the names of his housemates as easily as if he were telling you who was at last Saturday night's poker game: "Let's see, there were 11 of us. I roomed with Bob Joy, Buzz Lind, John Rose and Lowell Olson were down the hall. Then there was Harry Miller ... Bill Elliott. ..."

Residential life for medical students in the early 1950s fostered a camaraderie that has endured well beyond that triumphant moment when they received their diplomas. Despite, or perhaps because of, arduous studies and living conditions that can best be described as austere, graduates of 1954 recall those days with the warm affection of soldiers bonded by the rigors of boot camp.

Recollections of that time, which ended with the opening of the Edward S. Harkness Memorial Residence Hall in the fall of 1955, live on in a class book assembled by the Class of 1954 in preparation for their 50th reunion next spring. Robert P. Hatch, M.D. '54, edited the class book.

"We loved the place," Crovatto says of his first New Haven domicile. (When her boarders told her about a broken toilet seat, Ma Levin responded that it was for "half-assed doctors. The name—'home for half-assed doctors'—stuck.") Ma Levin's boarders may not have known their host's first name, but the house rules were never in doubt. "She wouldn't tolerate women. Wouldn't let them in the front door," Crovatto recalls. Everyone knew Ma hoped her niece Jackie would marry a medical student, so whether this prohibition was a reflection of her moral code or just a desire to lessen Jackie's competition was not known. "Only once in my life have I found a bottle of wine so bad that I couldn't drink it. It was a bottle of something Ma Levin's niece tried to share with us," recalls Lowell E. Olson, M.D. '54. "But it was a nice place to live. We all got along well."

For \$8 a week, Levin's tenants got a room, housekeeping service, clean sheets and Sunday breakfast. They ate the rest of their meals at Nick's or one of the other greasy spoons that lined Congress Avenue. Dinner cost about 50 cents, and students often worked in the restaurant in exchange for food.

But the big treat for those who stayed at Ma Levin's was access to something rare and wonderful—television on Sunday evenings. "I'd never seen TV before. We'd all get together and watch *Your Show of Shows* with Sid Caesar," recalls Harry C. Miller Jr., M.D. '54. "She was like a surrogate mother to us."

Although Ma Levin's boarders enjoyed the homey atmosphere, they were usually eager to move into one of the medical school dormitories farther down Howard Avenue (where the children's hospital now stands). The cost was between \$5 and \$8 per week for a single room and between \$3 and \$5 per person for a double. But the main allure was a chance to interact with the more advanced students and to learn from their experiences. Plus, there were fewer rules. "I liked it better," says Crovatto. "You were absolutely free to do what you wanted, as long as you didn't burn the place down," which probably wouldn't have been hard to do. Adds Miller: "I remember a guy was locked out of his room, so he just broke through the wall."

Some students had radios or phonographs for entertainment. "I brought a stack of very precious first-edition 78s I'd collected: Glenn Miller, Tommy Dorsey," says Miller. "When I left med school I foolishly didn't take them with me. Somebody probably used them as Frisbees." As for access to telephones, "It wasn't a big deal in our lives," says Miller. "I can't even remember. There may have been a pay phone somewhere." One thing everybody remembers vividly was the formal tea hosted by faculty wives four days a week. "The tea was poured from a samovar, with cups, saucers, spoons, little cakes, the whole bit," says Crovatto. "Everyone came—faculty, nurses, students, house staff. It was a wonderful tradition." Less charming, but arguably more timeless, were the loud parties on the back porch of the dorm. Crovatto recalls



Members of the Class of 1954 gathered outside a rooming house on Howard Avenue, sometime in the 1950s.

a particularly boisterous gala involving fireworks after the board exams. "There was a convent right behind us. Usually the sisters were very tolerant, but this time they called the police."

The Class of 1954 included three women. Two lived off campus, and one, Eva H. Henriksen, M.D. '54, lived with women from the public health program in a dormitory next to the men's building. Consequently, dormitory life for her was significantly different than it was for the men.

"We were allowed to study together, to help each other, so the guys would get together in their dorm," Henriksen says. "But I wasn't going to go next door to study with them. You just didn't do that in those days. I wasn't a great med student, but I did it all myself." Henriksen did find a way to "visit" with one student in the men's dorm. "The space between his window and mine was just close enough that if we both leaned out, I could hand him a cup of tea," she recalls. "Then he'd hand me his mother's home-baked black walnut cookies."

Also outside the mainstream housing experience were World War II veterans, who lived with their wives and children in Armoryville, a village of metal half-cylinder Quonset huts built by the Army near the Yale Bowl. Two couples occupied each hut, one couple at each end, with the two apartments separated by a thin wall. "In the winter, whether you were warm or cold depended on which way the wind was blow-

ing," says Richard D. Pullen, M.D. '54, a Navy veteran. The apartments, which rented for \$37 a month, were heated with a pot-bellied coal stove and cooled by a sprinkler on the roof. "Silvia Heap, the wife of Walker Heap, put a can of frozen orange juice on the counter to thaw," recalls Hatch. "When she came back a few hours later, it had exploded in the heat." Hatch's other vivid recollection is that "the walls were quite thin, so you pretty well knew what activity was going on next door. It was kind of intimate that way."

While football games at the Bowl provided entertainment for veterans and their wives, they could also be a hardship. Either the couples were hounded by tailgaters wanting to use their bathrooms, or the roads leading to their homes were blocked off by traffic police. Getting to and from the medical school was also a challenge. Hatch remembers commuting for a while on an "old rusty bike I'd picked up somewhere." Armoryville couples usually walked, biked, took the bus or used vintage Plymouths or Fords. "It might have been hard, but I remember it as a happy and fulfilling time," Hatch says.

Indeed, whether home was a Quonset hut, a dormitory or a rooming house, the memories of former occupants have acquired the patina of nostalgia. "Things happen in your life that are life-changing. My going to the Yale Medical School was one of them," says Crovatto.

—Jennifer Kaylin

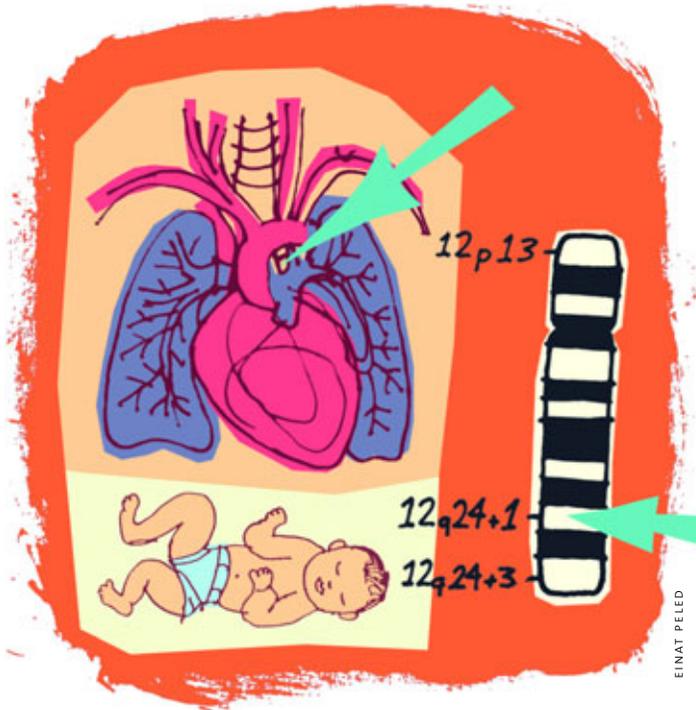
Journey of the heart

By Trisha Gura

A collaborative bridge between Yale and Iran spanning the genetics of cardiovascular disease is a two-way street for science.

Children in Iran face an elevated risk of patent ductus arteriosis, a congenital heart defect in which a critical blood vessel in the heart does not fully seal after birth.





Researchers from Yale and the Iran University of Medical Sciences in Tehran believe a gene mutation on chromosome 12 causes at least one-third of patent ductus arteriosis cases in Iran and may be responsible for as many cases in other populations throughout the world.

Every medical student must struggle to fight off distractions, but Arya Mani, M.D., had to contend with more than his share. Just before he began medical school in his native Iran in the late 1970s, the nation's capital, Tehran, was rocked by a massive, student-led uprising that made headlines around the world. The Ayatollah Khomeini ousted Mohammad Reza Pahlavi, who had ruled the nation as the Shah of Iran for nearly 40 years. Khomeini rose to power on the wings of an impassioned revival of Islamic fundamentalism, and toward the end of 1979 he began a nail-biting 444-day stand-off with the United States over the capture of hostages from the American embassy, an incident which continues to have profound political repercussions today.

Mani did his best to keep his mind on his studies against the increasingly tense political backdrop in Iran, but in the midst of the upheaval his university was closed, and he fled to the Johannes Gutenberg-University of Mainz in Germany to complete his training. In the last leg of a long journey, he arrived at Yale as a hospital resident in 1992, and he has made New Haven his home ever since.

Mani, now a cardiologist and assistant professor of medicine, had long been convinced that genes play a critical role in many forms of heart disease, but he hadn't had an opportunity to do serious research in the area until he became a chief resident at Yale in 1993. He then found an enthusiastic and like-minded mentor in Richard P. Lifton, M.D., PH.D., who has spearheaded an innovative series of genetic research projects around the world, including groundbreaking research on the genetic basis of hypertension. Mani returned to his homeland in 1998 as part of a globe-spanning collaboration between New Haven and Tehran. By bringing Yale's state-of-the-art genomics initiatives to bear on the time-honored marriage customs of Iran, Mani's work has put the Lifton lab within striking distance of an elusive gene or genes that act to cause a common congenital heart condition.

A novel approach

In his science, Lifton, the chair and Sterling Professor of Genetics, believes in going to extremes. Find genetic culprits at the pathological and geographical edge, he says, and you can apply your insights to the norm. Thus he has investigated families with the very highest and lowest blood pressure to find clues to treat the everyday hypertension that affects the rest of us.

Populations in which marriages between close relatives are common are particularly ripe for study, says Lifton, a Howard Hughes Medical Institute investigator, because intermarriage keeps the same genes circulating within the group, and genetic diseases occur more frequently. For example, first cousins are much more likely to carry identical defective recessive genes passed down from a grandparent. If these cousins marry, their children run a higher risk of genetic dis-

ease than children in more diverse populations. And the more such illnesses arise in a small, discrete population that practices intermarriage, the easier it is to spot recessive genes that may be responsible. On any given day in his third-floor lab in Yale's new Anlyan Center, Lifton might be found poring over pedigrees of a Saudi Arabian village, a family in the Italian Alps or a close-knit clan in the South Pacific.

The approach has paid off: to date, members of Lifton's lab have unearthed more than a dozen genes involved in the regulation of blood pressure and several other genes underlying conditions ranging from osteoporosis to vascular disease of the brain.

Mani knew that 25 percent of live births in Iran arise from parents who are closely related, so he thought that the country could provide a uniquely valuable setting to apply Lifton's methods. He proposed to travel to Iran to conduct a systematic study of disease patterns in families with closely related marriage partners. Lifton advised Mani to first identify any diseases that are markedly more common in the general Iranian population than would be expected from his clinical experience at Yale, and to then look for a subset of those illnesses that occurs frequently among children of closely related parents.

To prepare for the journey, Mani searched the medical literature and discovered a research paper written by Shahrokh Naderi, M.D., an Iranian gynecologist, in 1979. Naderi had catalogued several diseases that were more common in Iranian children of closely related parents, including congenital heart disorders. Neither Mani nor Lifton was aware of any other reported association between intermarriage and cardiovascular disorders, so Mani contacted Naderi, who has also emigrated to the United States, for advice on following up this work in Iran. Mani also consulted with Iranian-born Tayebeh M. Rezaie, M.Sc., at the University of Connecticut Health Center in Farmington, who had been studying genetically based illnesses in Middle Eastern populations. Rezaie provided Mani with a list of candidate illnesses, including the congenital heart defect called patent ductus arteriosus, or PDA.

The ductus arteriosus is a normal fetal structure that joins the aorta to the pulmonary artery; since the fetus obtains oxygen from the placenta, the ductus arteriosus allows blood to bypass the lungs to supply the rest of the body. In PDA, the ductus arteriosus does not fully seal off after birth, and some oxygenated blood in the aorta returns to the lungs via the pulmonary artery instead of entering the general circulation. Many children with PDA experience nothing more than a mild heart murmur or tiredness and are not properly diagnosed for two years or more, but some infants with PDA must be rushed to emergency rooms, where surgeons repair the defect to prevent congestive heart failure.

Mani had seen patients with severe PDA symptoms in his rounds at Yale. But American physicians weren't certain that the condition had a genetic cause because it appears so

sporadically in the United States and, more often than not, does not seem to affect PDA patients' relatives. Though this clinical picture is typical of recessive illnesses masked by a genetically diverse population, the consensus was that PDA is caused by unknown environmental triggers.

Politics often trumps science, and there were particularly worrisome political hurdles facing Mani in his quest to do research in Iran. Relations between the United States and Iran were severely strained by the 1979 hostage crisis, and have been mixed at best since then. Though there have been instances of cooperation, such as the recent U.S. aid to Iran in the aftermath of the earthquake in the city of Bam (See sidebar, page 29), President Clinton instituted a strict trade embargo against the country in 1995, and President Bush famously named the country in his 2002 State of the Union address as part of an "axis of evil." Fortunately for Mani, Asghar Rastegar, M.D., associate chair for academic affairs in the Department of Internal Medicine, had been building medical partnerships between Yale and countries in need, including Iran, for a dozen years.

After the fall of the Soviet Union, Rastegar, an Iranian by birth, organized collaborative efforts with Russian educators, arranging faculty exchanges and trips to Russia for Yale researchers. With the announcement of Clinton's trade embargo, Rastegar again sought to build scientific bridges. "I felt that Iran was being isolated politically," he says, "but that such isolation should not extend academically." For example, Rastegar has sponsored Iranian faculty members to spend sabbaticals at Yale and more recently he has helped to set up partnerships between Iranian physicians and two Yale researchers—Richard S. Schottenfeld, M.D. '76, professor of psychiatry and master of Davenport College, and David A. Fiellin, M.D., associate professor of medicine—to study issues related to substance abuse and HIV in Iran.

Introductions in Tehran

Rastegar, who had known Mani from his student days during the Iranian revolution, acted as Mani's go-between with Iranian physicians and scientists, so when Mani arrived in Iran he was able to quickly team up with internist and nephrologist Behrooz Broumand, M.D., at the Iran University of Medical Sciences in Tehran. Broumand was keenly interested in genetically based kidney diseases and was eager to learn techniques to ferret out the precise genetic defects underlying these conditions. However, he says that he and other physicians at Iran's top hospitals are handicapped by the country's economic struggles and political isolation. "We have a shortage of basic science knowledge in Iran because of the lack of facilities," Broumand says.

According to Broumand, only about 5 percent of Iran's gross national product goes toward health care (compared to 13 percent in the United States), and many hospitals do not have essential medical equipment such as CT or MRI

machines, let alone facilities for basic research. The physicians who staff Iran's hospitals carry very heavy patient loads but are usually paid only about one-tenth the salary of their colleagues in private practice.

"They really had to be devoted to work in the hospital," Mani says. But the doctors he met at Tehran's Shahid-Rajai Cardiovascular Medical Center at the Iran University of Medical Sciences were anxious to help him with his work, and appeared to be motivated more by a thirst for knowledge and a desire to train with new technology than by financial compensation. Such physicians formed the Iran-based part of Mani's team, and once they provided him with patient records and recounted their clinical experience with Iran's close-knit families, it didn't take long for him to conclude that the University of Connecticut's Rezaie was right—PDA in Iran had all the earmarks of a promising candidate illness for genetic analyses.

Lifton still recalls a phone call Mani made to Yale from Tehran. "He told me, 'I have seen 20 cases of PDA here in two weeks but only half a dozen in my entire clinical experience at Yale.'" The patient records painted a startling picture: at Shahid-Rajai, PDA accounted for 15 percent of 13,000 congenital heart defects, while the best estimates say that PDA makes up only 2 to 7 percent of congenital heart disorders in the United States. And the disease showed up far more frequently in children whose parents were first cousins. When the researchers looked closely at 338 recent cases of babies born with PDA, nearly two-thirds had closely related parents.

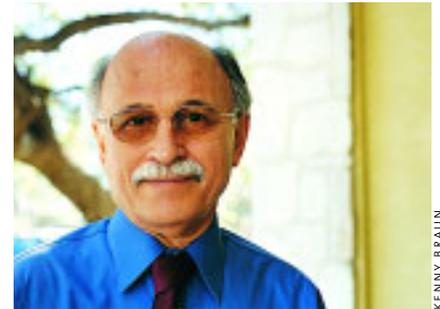
These data indicated that, at least in Iran, the disease is almost certainly caused by a defect in one or more recessive genes.

Mani collected blood samples from 21 PDA patients born to parents who were first cousins for genetic analysis back at Yale. Members of Lifton's lab combed through the patients' DNA and compared it to samples from unaffected children, performing analyses that mark stretches of the genome where genetic defects might lie. The lab's preliminary analyses pointed toward three chromosomes as culprits, but more intensive number crunching eventually steered the group toward a section of chromosome 12; nine PDA patients had sequences in this region that were so similar that the odds of the matches occurring by chance are less than one in a million. In a November 2002 paper in the *Proceedings of the National Academy of Sciences*, Mani and Lifton proposed that a gene mutation somewhere in this section of chromosome 12, which they have christened PDA1, causes at least one-third of the PDA cases in Iran, and may be responsible for as many cases in other populations throughout the world. The study is further vindication of the cross-cultural methods that Lifton has so profitably used thus far.

"This is a very interesting approach, and one that will be even more powerful in the near future," says molecular geneticist David M. Altshuler, M.D., Ph.D., of the Broad Institute in Cambridge, Mass. In particular, Altshuler says that the approach of Mani and Lifton benefits from a new genetic tool called a haplotype map—in essence, an exhaustive inventory of common DNA variations within human



TERRY DAGRADI (2)



KENNY BRAUN

LEFT TO RIGHT Arya Mani returned to his native Iran to seek out diseases with a genetic cause. Back at Yale, Richard Lifton's analysis of DNA led to a section of chromosome 12. Behrooz Broumand teamed up with Mani in Iran to seek out genetic underpinnings of disease.

populations. Knowing those variations will give geneticists such as Lifton a head start in identifying DNA patterns that might be linked to diseases.

Putting science over politics

Members of the Yale-Iran PDA collaboration still work together, but they are also heading in different directions. Lifton and his colleagues are whittling away at millions of base pairs on chromosome 12 to find the gene that carries the mutation that causes PDA. So far, they have ruled out three promising candidates, but there are 31 more to test. Lifton is also applying his methods to other diseases found in different isolated populations; for example, he is now on a hunt for the genes that confer a high risk of heart attack among the people of the Kosrae Islands in the South Pacific. Meanwhile, Mani and Lifton have begun work to uncover the genetic underpinnings of the high risk of early heart attack in Indian men, which seems to persist even if these men leave India to live elsewhere.

As for Broumand and his Iranian colleagues, they are building on the training Mani gave them by collecting tissue samples from adult heart disease patients born of closely related parents in the hopes of finding genes related to that ailment. In the end, the New Haven-Tehran collaboration was a win-win situation, Broumand says—America has cutting-edge genomic technology, and Iran has unique study populations. If the two countries continue to join forces, he says, science can more rapidly find the treatments that patients so desperately need.

But Broumand does voice one note of caution. Many of the Iranian patients who participated in the study did so, he says, because they hope that they or their descendants will eventually benefit from any treatments that emerge. Similarly, Iranian physicians donated their time to expand their knowledge and to better treat their patients. Broumand fears that those in poorer nations who help to make cross-cultural medical collaborations possible could be forgotten once the necessary data are gathered. “If the studies stop at the point when the paper is published, then the fruit is dead and nothing else will happen,” he says. For his own part, Lifton has been inviting researchers from Iran and other countries to spend time training in his lab and to take knowledge back to their home countries.

Broumand believes that everyone can benefit if Western researchers maintain strong contacts with colleagues in other regions, not simply by reading each others’ papers, but by engaging in regular discussions with each other. And this is particularly true where the United States and Iran are concerned. “I believe that if we go through cooperation in science,” he says, “we will create an environment to soften the politics and the violence, which is based on politics. That is the hope.” **YM**

Trisha Gura is a science writer in Brookline, Mass.



In earthquake’s aftermath, Yale physician makes a journey back to Iran

Five days after an earthquake devastated the Iranian city of Bam in December, Asghar Rastegar, M.D., professor of medicine and associate chair for academic affairs in the Department of Internal Medicine, was on an AmeriCares cargo plane carrying 80,000 pounds of emergency supplies. His mission was to help deliver the supplies and assess the city’s medical needs for the next two to three months. Rastegar was asked to help because he is originally from Iran and had worked with AmeriCares on relief efforts after a 1990 earthquake there. And he’s familiar with the area, having taught at the medical school in Kerman, the provincial capital 120 miles from Bam.

“It was a very peculiar feeling,” he said of the approach to Bam.

Roads were open and there were no immediate signs of devastation. “You enter the city and after two blocks everything is destroyed.”

The earthquake, which struck at 5:30 a.m. on December 26, destroyed most of the city, including its two hospitals. The death toll was at least 43,000. Most of the city’s health workers were killed, leaving no one to treat the injured during the crucial eight hours following the earthquake. Although physicians and nurses from Kerman and other nearby cities filled the gap heroically, Rastegar said national planning for the earthquake was missing. “Iran sits on a major earthquake fault,” he said. “This is going to happen again.”

Now Iranian officials, working with Iranians who live in the United States, are planning meetings to prepare an emergency response plan.

—John Curtis

Two alternatives, each a little wrong

With that definition of a dilemma in mind, Yale's cadre of bioethicists wade into our mailbag and weigh in on readers' questions from the front lines of medicine.

By Marc Wortman
Illustrations by Serge Bloch

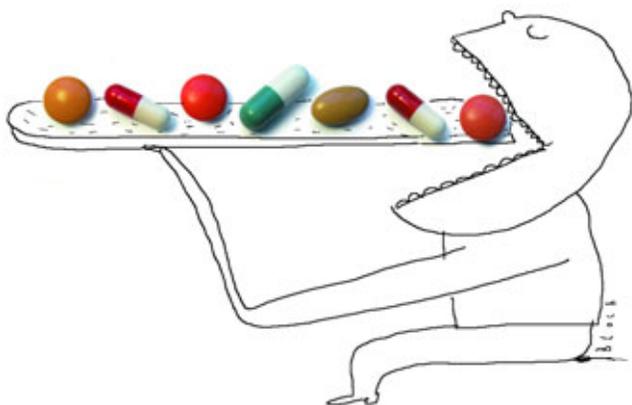
In the 1980s, neurosurgeon Dennis D. Spencer, M.D., HS '77, was a leader in an investigational effort at Yale to transplant fetal cell tissue in the brains of Parkinson's disease patients. Animal studies had shown that implanting the cells might reverse the tremors and other neurological problems caused by the disease. His research team applied for a grant from the National Institutes of Health (NIH) to carry out some of the first studies in humans. Unlike other teams applying for the grants, Spencer's group refused to include placebo surgery as part of their study. The sham surgery would have required him to carry out all the steps of the transplant surgery—drilling a hole through a patient's skull and inserting a needle into the hole—but without delivering any fetal cells. "My reading of the literature," he now says, "showed that any placebo effect from surgery would have been short-lived. We believed that over time you could clearly judge the efficacy of the procedure without subjecting patients to an unnecessary risk. We felt to do so would be unethical." NIH insisted on the placebo surgery. "We didn't get funded."

For Spencer, who is now interim dean of the School of Medicine, that experience marked the beginning of his need to study bioethics in a more focused way. "I started reading the literature on the ethics of using surgery as placebo. I read what happened in the past and that helped crystallize the issue for me." He and his colleagues began a series of debates on the subject at NIH and neurosurgical society meetings. "For scientists, study controls and placebos are important, but you need to consider the ethical issues." While no formal policy on placebo surgery resulted, "We got people to think about it."

The need to think about, explore and, when possible, resolve such complex issues has increased at Yale and elsewhere as medicine has become more complex. Spencer is one of many Yale physicians who regularly encounter ethical challenges in their work. They have a number of resources available to advise them when necessary. The Yale-New Haven Hospital Bioethics Committee—a panel of physicians, nurses, lawyers, social workers, clergy, ethicists and community members—reviews dilemmas, sets guidelines for care and also looks into issues about the quality of hospital services and physician conduct. "As professionals," says Thomas P. Duffy, M.D., professor of medicine and a founding member of the Bioethics Committee, "we have an obligation to monitor how all of us are performing as physicians. The actions of one reflect on all of us."

When urgent bioethical dilemmas requiring swift, high-level decision making arise, physicians can turn to the hospital's chief of staff, Peter N. Herbert, M.D. '67, HS '69, and attorneys for final arbitration. Any Yale investigator seeking to carry out experiments involving human subjects must file an application with one of four university institutional review boards that oversee the studies, based on federal guidelines. A variety of other departmental committees and individual experts are also available to help resolve disputes when they occur. "Ethics," says Robert J. Levine, M.D., HS '63, professor of medicine and a co-founder of the hospital ethics committee, "is civilized society's alternative to violence in dispute resolution."

Levine is co-chair of Yale's Interdisciplinary Bioethics Project and director of the Donaghue Initiative in Biomedical



Dilemma 1

Is it ethical to help a patient against his will or when he doesn't know or understand his situation?

and Behavioral Research Ethics at Yale. He points to the Greek origins of medical ethics as what he terms “a field for developing standards for behavior that is praiseworthy or blameworthy.” However, he also defines an ethical dilemma as one in which there are “two alternative courses of action, each of which is a little wrong.”

Disputes arise because opposing responses are possible. Nonetheless, dilemmas require resolution if the needs of individuals and society are to be met. Last autumn, *Yale Medicine* invited its readers to submit biomedical dilemmas they have encountered in the course of their work, and many of you responded with issues where a proper course of action was not necessarily obvious. Issues ranged from a family that insisted for religious reasons that a loved one who was suffering not receive pain medication to concerns about the professionalism of colleagues.

Working with Levine, Contributing Editor Marc Wortman and the editors of *Yale Medicine* selected four provocative and difficult-to-resolve dilemmas. Individual faculty members with relevant expertise were invited to reflect on one of the dilemmas and to present their views of the logic of a resolution. The dilemmas are presented anonymously but are based on real situations described by readers from around the country. **YM**

Marc Wortman is a contributing editor of *Yale Medicine*.

A young man with schizophrenia and a history of non-compliance with treatment was admitted to my outpatient practice in a severely psychotic condition. He was completely lacking insight into his condition, and all approaches to gain compliance—most importantly, taking medications that could reduce his psychotic state—failed. His mother convinced me to prescribe medication, which she secretly placed in the patient’s food for nearly two years. I saw the patient for medication checks regularly, but he was unaware of his “compliance” throughout this time. This strategy resulted in slow, steady and quite remarkable improvement in all areas of functioning. The only untoward event, if you will, was the patient’s return to a pattern of partial compliance and eventual return of some symptoms several weeks after I chose to tell him the entire story. I had simply grown too uncomfortable with the situation, realized that this could not go on forever, and hoped that his clinical improvement just might allow him to embrace a proven, efficacious treatment (which was the ultimate plan discussed with his mother prior to embarking on treatment). Despite some decline in his condition and only partial compliance, the patient continues today improved from admission and much more amenable to inducements to adhere to his regimen. I believe I have given this individual a fighting chance where there was none—yet I have been acutely aware of the ethical dilemmas in his treatment along the way. Was I right to pursue this course? “A person with schizophrenia, such as this patient during psychotic exacerbations, may not be capable of making a variety of decisions and may require guardians to look after their interests. Guardians, however,

may not force medications on outpatients in Connecticut,” says Howard V. Zonana, M.D., professor of psychiatry and head of that department’s forensic psychiatry residency program. “Patients frequently don’t like to take medications. They have some unpleasant side effects. As part of their illness, some patients don’t believe they’re sick.” Zonana chaired the YNHH Bioethics Committee from its inception in 1985 until 1999.

He notes that psychiatrists are not alone among health care providers in receiving requests from one family member that they deceive another about care being given. For instance, physicians in family practice may encounter patients with sexually transmitted diseases who request that the doctor treat their spouses surreptitiously because they are afraid of threatening their marital situation. To hide information from one patient for the sake of another, he says, “is putting the needs and beliefs of the person who wants to keep the secret first and is conspiring in a deception. The doctor who does so is making complicated value judgments and is being co-opted. Sometimes, as in a case like this, it may work out, but there are many more times when it won’t, and the price for a betrayal of trust is very high, threatening both the present and future physician-patient relationships.”

Zonana, medical director for the American Academy of Psychiatry and the Law, helped to write the state of Connecticut’s civil commitment statutes. Psychiatrists, he points out, operate under extensive legal regulation because they have powers akin to those of the police to detain a mentally ill person involuntarily. He says, “There are many chronic schizophrenics on the street, and we don’t go around surreptitiously injecting them with syringes of medications. There’s always a balance between individual autonomy and social needs and health. If somebody becomes gravely disabled or dangerous, the person loses some autonomy. There is always a dilemma about what values the individual and a community hold more primary. In this case, I don’t see the clinical situation compelling enough to justify this deception.” He contends that there are other ways to help someone gain insight into his or her condition. “The doctor’s intent was clearly humane, but I think in the long run honesty trumps health outcomes. I would not have been willing to do this.” ■

Dilemma 2

**Human subjects research:
when is use of a placebo
ethical?**



There are several standard drug therapies that can help prevent vertebral fractures in some women with osteoporosis, a potentially serious problem associated with a condition common among aging women. A pharmaceutical company asked me to design and direct a study of a new medication that shows promise of preventing fractures in many more women. I designed the study to compare the new drug with placebo, in which neither the clinician nor the patient would know whether she was receiving the drug or a pill having no effect. Based on statistical analysis, the proposed trial could not show the new drug's effectiveness until the number of new fractures in the placebo group exceeded by 150 the number in the group receiving the new drug.

Our hospital's institutional review board, or IRB, rejected the study, claiming it would be unethical to treat patients with a placebo when there are standard therapies that are known to be at least partially effective. The review board suggested that, instead of placebo, we give the control group one of the standard therapies. I disagreed because most women who have osteoporosis do not receive such treatment, particularly when they have no symptoms. (The women to be recruited for this study will have no symptoms of osteoporosis.) Furthermore, most vertebral fractures complicating osteoporosis have no symptoms, and the women who have such fractures often don't even know it; it's not as if they have serious pain or disability. Moreover, it will still be necessary to continue the trial until the number of new fractures in the control group exceeds by 150 the number in the group receiving the new drug. The same number of women will experience this injury; it will just take a lot longer to reach that number. In other words, there would be a substantial loss in efficiency of the trial with no compensating benefit. Was the review board's action right in this case? As chair of the Human Investigation Committee at the School of Medicine for 30 years until 2000, Professor of Medicine Robert J. Levine, M.D., HS '63, was called upon to review hundreds of applications for testing new therapies. He is the author of the widely used book *Ethics and Regulation of Clinical Research* and founding editor of the journal *IRB: A Review of Human Subjects Research*. He agrees with the review board's decision. "When a therapy known to be effective already exists, even if only partially beneficial, and withholding the effective standard may result in serious complications, it is unethical to use placebo."

Levine suggests that the physician consider an alternative study using what he terms an "add-on" design for the trial. This is possible when a new drug acts by a different mechanism than the standard drugs currently used in medical practice. In osteoporosis, one of the standard therapies, a combination of vitamin D and calcium, is partially effective in the prevention of new fractures, according to Levine. Since vitamin D/calcium works differently in the body than the new drug, he believes it would be appropriate to give this combination to all patients and also give half of the patients the new drug and the other half the placebo. "In this way," he says, "the trial has the advantages of being a placebo-controlled study without depriving the women of a known, partially effective therapy." Although it will still be necessary to continue the trial until the number of new fractures in the control group exceeds by 150 the number in the group receiving the new drug, Levine believes the loss of efficiency will be compensated by the therapeutic benefits to the participants getting the placebo. "If I were on that IRB, I would approve such a study." ■

Reunion program highlights ethics

"Bioethics in the 21st Century," a discussion focusing on the contributions of alumni, faculty and students at the School of Medicine, will be the subject of an Alumni Reunion Weekend program June 5 from 9 to 11 a.m. in the Anlyan Center Auditorium, 300 Cedar Street. The panel will be moderated by Robert J. Levine, M.D., HS '63, co-chair of the Interdisciplinary Bioethics Project at Yale.

The panelists and their topics are: Thomas P. Duffy, M.D., "Ethical Aspects of Medical Professionalism in the 21st Century"; Rupali Gandhi, J.D. '00, M.D. '04, "Children as Research Subjects: Ethical and Legal Issues"; Tia Powell, M.D. '87, "Cultural Competence in Medical Ethics: Notes from Japan"; and Philip R. Reilly, J.D., M.D. '81, "Emerging Ethical Issues in Genetic Medicine."

Dilemma 3

When is extraordinary life-saving care appropriate?



A baby boy was born at full term but via an emergency Cesarean section, with a mysterious, intense skin reddening. Immediately following birth, he was put into the pediatric intensive care unit in the hospital where I work. Over the next three days, he had multiple organ failures—of the myocardium, lung and liver. On his fourth day of life he had a major seizure. Studies showed intracranial bleeding, described by the pediatric neurologist called in to see him as “the worst I’ve ever seen.”

The baby was transferred to a medical center where he received extensive evaluation and supportive care. The family decided on a “No Resuscitation, No Extraordinary Measures” order and made that clear to the doctors. No cause for the bleeding or other aspects of his condition was ever found. The outlook presented to the family by pediatricians was very grim, and he was not expected to leave the hospital.

Still in the first week of life, the boy was not swallowing well and was regurgitating so often that a Nissen operation was considered. This procedure cinches up the esophageal-gastric junction to prevent gastric reflux. The family approved the surgery, but unknown to the family, the surgeon also inserted a gastric feeding tube brought out through the upper abdomen. Given nourishment via the feeding tube, the child began to hold his own and gradually improve over a period of several weeks.

Today the child is a couple of years old and weighs around 30 pounds. He is still fed through the tube, never swallows, has no excretory control, has never rolled over, cannot sit up, receives anti-seizure medication, makes no purposeful movements other than occasional random arm waves, does not crawl, does not speak or respond to commands and basically has an IQ of zero. His medical bills have totaled nearly \$1 million so far, with the local county government bearing most of that cost. The family is responsible for the insurance copayments, incidental care and other costs amounting to more than a third of the family’s income.

A young family is blessed with a son, but burdened with that son being a clearly nonfunctioning human being. “Miracles” do occasionally happen in medicine, but there is no miracle for this unfortunate family. The question is, what should have been done and what should not have been done? “There is no legal or theological basis, in Catholicism, Judaism or the majority of Protestant faiths, for keeping alive by artificial means someone for whom there is no possibility of recovering,” says Sherwin B. Nuland, M.D. ’55, HS ’61,

At Yale, a growing focus on bioethics

A biting wind blows through the darkened Yale campus on a cold December night. The irony of the end-of-the-year gloom is not lost on the 25 members of the End-of-Life Issues working research group meeting in a seminar room at the Institution for Social and Policy Studies (ISPS). This night, four staff members from the Connecticut Hospice in Branford speak about the stresses faced by caregivers for the dying. The audience is composed of students; faculty from the medical, divinity and nursing schools, as well as faculty from other academic institutions; and local community members.

During the discussion that follows, Fred A. Flatow, M.D., a former oncologist who is now a hospice physician, notes the challenge that doctors newly arrived from traditional hospital settings frequently encounter switching from one mode of care to another. "They are always looking to treat a disease," he said. "We tell them they have to treat the patient, not the disease." The group then launched into a debate over the differing and sometimes conflicting emotional qualities and approaches to patients that caregivers need to succeed in each medical setting.

That sort of investigation into the nature and impact of

medical care and research goes on somewhere on campus almost every day. The group meeting this evening is just one of 15 different working research groups, in bioethics that hold monthly meetings on topics ranging from technology and ethics to allocation of health care. The various groups as well as publications, seminar and speaker series and visiting professors, are part of the burgeoning Interdisciplinary Bioethics Project at Yale.

Launched in the summer of 1997 by the ISPS to bring together the swelling numbers of people interested in the field, the bioethics project has drawn more than 500 participants to its programs from departments across the university, the local community and the larger world of academia and health care. "The project is fluid and that accounts for its popularity," says Carol A. Pollard, associate director of the bioethics project at the ISPS, who coordinates the project's many activities. "People come to ask why we don't do something in an area with an underlying ethical question. They can then work with us to make it happen."

Those efforts received a major boost last year when the Patrick and Catherine Weldon Donaghue Medical Research Foundation awarded the Bioethics Project a five-year, \$2.1 million grant. According to Robert J. Levine, M.D., HS '63, professor of medicine, and Divinity School Professor Margaret A. Farley, PH.D., co-chairs of the Bioethics Project, part of those funds will go toward community outreach, including a statewide network of institutional review boards, the hospital and medical center ethics watchdog committees that oversee biomedical and

behavioral research. The grant also helps to bring a prominent bioethicist-in-residence to Yale each school year. This year's visiting faculty member is David H. Smith, PH.D., a professor of religious studies at Indiana University, where he is immediate past director of the Poynter Center for the Study of Ethics and American Institutions. He is currently at work on a book on religion and the morality of care for the dying. At Yale, he is teaching popular courses to undergraduate and graduate students on bioethics and also directs the End-of-Life Issues working research group for the year.

Many of the working groups focus on policy issues and have become voices in wider public debates. "It is in the nature of biomedical ethics," says Levine, "that almost anything is potentially related to public policy."

Several of the Bioethics Project's groups have taken on a life of their own, developing their own visiting-speaker series and seeking outside support for their efforts. One of the larger groups, the Stem Cell Interest Group, was founded in May 2002 by medical student Rajesh Rao with stem cell scientist Diane S. Krause, M.D., PH.D., associate professor of laboratory medicine and pathology, as an advisor. The group has grown from 15 to 150 members

from a wide range of disciplines. It has brought speakers to Yale including leading stem cell investigators and Christopher Reeve, an advocate for more research in the field. The group now hopes to establish a multidisciplinary program, with medical and ethical research and education as components.

Most of those involved in the working groups are not formally trained as bioethicists. Interim Dean Dennis D. Spencer, M.D., HS '77, who attends meetings of various study groups, has spoken on bioethics as part of an annual guest lecture series on the field held at the Joseph Slifka Center for Jewish Life at Yale. "I am not a bioethicist per se," he says, "but as a neurosurgeon, I'm engaged in it in the trenches. Most of us consider ethics to be common sense. All you need to do is ask a resident a tough ethical question and you see that it is not just common sense. We all bring baggage and a set of beliefs that you have to get rid of in approaching these issues. You have to acquire a basis to argue your views rationally."

A member of the End-of-Life Issues group, Stanley H. Rosenbaum, M.D., professor of anesthesiology, medicine and surgery, agrees. "I spend so much energy dealing with acute medical problems. This helps me step back and consider the justice and ethical aspects of what we do."

—Marc Wortman

clinical professor of surgery and author of *How We Die: Reflections on Life's Final Chapter*. He points out that in the landmark 1976 Supreme Court case of Karen Ann Quinlan, who was in a persistent vegetative state and whose parents had sought for her to be removed from life support, her priest and the local bishop believed that she should be allowed to die. (Removed from life support, she lived on in that state until her death in 1985.)

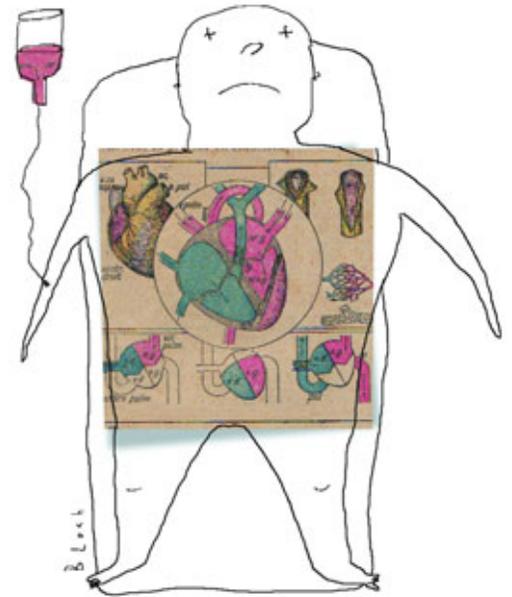
A founding member of the Yale-New Haven Hospital Bioethics Committee, Nuland notes that fear of legal ramifications often drives doctors to pursue extraordinary means to keep their patients alive, sometimes even in violation of expressed patient and family wishes. The courts have consistently supported patients, their families and physicians who choose not to have “heroic” measures taken to keep a loved one alive. “I think fears of legal repercussions are unfounded,” he says. “The medical team needs to make clear the various scenarios if they do or do not intervene. Then it all gets down to the wishes of the patient or the closest kin. This was a violation of the family’s hope, and of their intentions for their child.”

He believes that the physicians erred at many levels. “There is no way for people of any knowledge to disagree about what this child’s outcome would be. There is no possibility that the physicians did not know this.” Nuland believes that, by pursuing surgical procedures, the pediatric surgeon violated several moral and ethical principles. “The only criterion for a treatment decision should be the patient’s welfare.” He suspects that the surgeon may have operated on the patient because the “case was a rare opportunity to improve his or her technical skills in operating on a tiny baby. He was prolonging this poor child’s life by carrying out procedures that make no sense whatsoever. The physicians knew this. This seems morally and ethically reprehensible.”

He believes that a physician must look at the goals of any therapy he or she undertakes. “They seem to have decided the goal was to discharge the patient from the hospital. To me the goal is what makes most sense for this family and this child.” ■

Dilemma 4

Is it ethical to continue life support in brain-dead patients so others may live?



I was working in a trauma room. A patient was brought in who had been shot through the head. Although he had vital signs, he was hemorrhaging rapidly through the wound. There was wide destruction of his brain tissue; much of it had spilled out on the stretcher. My immediate reaction was, “This poor person has died.” Any intervention at that point seemed futile. Then another doctor who was present ordered blood. I was shocked and asked, “Why?” The doctor replied, “Perhaps he will be an organ donor.”

We aggressively resuscitated a person who was demonstrably beyond saving with large volumes of blood, ventilator support and other means on the chance that we would find a family member in time to ask if he would be a donor. Was it right to treat the patient in front of us—who was functionally dead and moments from being without vital signs—as a potential source for an organ harvest? If the two physicians agreed that the patient could clearly not be saved, it would be ethically acceptable to stop treatment, according to Mark R. Mercurio, M.D., HS '85, co-chair of the Yale-New Haven Hospital Bioethics Committee and associate clinical professor of pediatrics, who also co-directs a bioethics seminar series for pediatrics residents. “However,” he adds, “that does not mean that continuing aggressive treatment with the goal of enabling possible organ donation was unethical.”

According to Mercurio, there are several ways of looking at the question. The patient-centered approach is perhaps the one most widely favored by medical ethicists. It holds that in the absence of any knowledge of the patient’s wishes, decisions should be guided by his or her best interest. To determine this, physicians must weigh the relative benefits and burdens imposed on the patient by a particular course of action. “Pain should always be considered as a potential burden,” he says. “Also, perhaps his family will be left with a much larger financial burden, which might be viewed indirectly as a burden to him.”

It may also be valid to consider the interests of others, including family members or society at large. While it may seem wrong to treat the patient just to serve someone else’s interests, keeping the patient alive for a period of time while important information is gathered might be appropriate. “Some ethicists feel that we do not need to restrict the analysis to the patient,” Mercurio states, “but can consider the interests of others affected by those decisions as well. Perhaps his family will draw some measure of comfort from organ

donation, and just as their cost may be perceived as his cost, their consolation may be seen as a benefit to him.” Such an analysis could, he suggests, be expanded still further to incorporate potential organ recipients or even a much wider set of people. “It seems the questioner sought adherence to a patient-centered ethic, but perhaps the other physician thought it reasonable to consider the interests of others. Ultimately it is a matter of opinion, not medical fact, which approach is more appropriate.”

Mercurio concludes that while the physicians may not have been ethically required to continue the treatment, “I do think it was ethically permissible for them to do so, at least until the patient’s status as a possible organ donor could be clarified. If they learn that he had not chosen to be an organ donor, and the family did not choose that for him, at that point I would then recommend ceasing further efforts to maintain vital signs.”

One final point: “When the correct course between two options is not clear, it seems to me the wiser choice is the one that is potentially reversible when more information becomes available,” says Mercurio. “This would also favor attempts to maintain vital signs until the patient’s and family’s wishes regarding organ donation could be clarified.” ■

What do you think?

The responses provided here by Yale faculty members address four problems that troubled readers of *Yale Medicine* because a proper course of action was not easily decided. What would you have done, faced with the same dilemmas? Send your thoughts to Letters, *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612, or via e-mail to yymm@yale.edu.



Pietro de Camilli



Daniel DiMaio



Steven Hebert



Arthur Horwich



Stefan Somlo

Five faculty members honored with endowed professorships

PIETRO DE CAMILLI, M.D., FW '79, professor of cell biology, has been named the Eugene Higgins Professor of Cell Biology. De Camilli, who is also a Howard Hughes Medical Institute investigator, leads a research program exploring the molecular basis for synaptic transmission.

DANIEL C. DIMAIO, M.D., PH.D., professor of genetics, has been named the Waldemar Von Zedtwitz Professor of Genetics. DiMaio is vice chair of the genetics department and director of the Yale Cancer Center's Molecular Virology and Oncology Training Program.

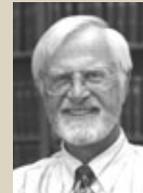
STEVEN C. HEBERT, M.D., chair and professor of cellular and molecular physiology and professor of medicine, has been named the C.N.H. Long Professor of Cellular and Molecular Physiology. Hebert studies the mechanisms and regulation of potassium, sodium and chloride transport by cells.

ARTHUR L. HORWICH, M.D., HS '78, professor of genetics and pediatrics, has been named the Eugene Higgins Professor of Cellular and Molecular Physiology. Horwich, a Howard Hughes Medical Institute investigator, studies proteins known as molecular chaperones and the mechanisms by which they assist in protein folding in the cell.

STEFAN SOMLO, M.D., FW '91, professor of medicine and genetics and chief of the Section of Nephrology, has been named the C.N.H. Long Professor of Medicine. Somlo heads a multidisciplinary research center at Yale that investigates polycystic kidney disease.



Myron Genel



James Jamieson



Keith Joiner



Becca Levy

Myron Genel, M.D., professor emeritus of pediatrics, has received the Joseph W. St. Geme Jr. Leadership Award, presented annually by the seven societies that constitute the Federation of Pediatric Organizations. The international award recognizes Genel's contributions to pediatrics and to the advancement of national health policy for children. Last year Genel was named chair of the Governing Council of the American Medical Association's Section on Medical Schools. The section, which has 600 representatives, gives U.S. medical schools a voice in the formulation of the association's policies. It has been involved in recent discussions on implementing the new clinical-skills portion of the national board exams.

James D. Jamieson, M.D., PH.D., was awarded the William Go Award by the American Pancreatic Association. The award is given to individuals who have made outstanding contributions to pancreatic studies. Jamieson, professor of cell biology and director of the M.D./PH.D. program at Yale, was honored for his leadership in national organizations, his academic achievements and his abilities as an educator.

Keith A. Joiner, M.D., M.P.H. '03, the Waldemar Von Zedtwitz Professor of Medicine, became dean of the University of Arizona College of Medicine, on March 1. At Yale Joiner was the associate chair of medicine, chief of the Section of Infectious Diseases and director of the Investigative Medicine Program. Joiner's group studied two parasites, one that causes central

nervous system infections in patients with AIDS and another that causes malaria. He joins the University of Arizona at the start of a major expansion, including a bioresearch institute and a medical research building.

Becca R. Levy, PH.D., assistant professor of gerontology, was named the 2003 recipient of the Margret M. Baltes Early Career Award in Behavioral and Social Gerontology by the Gerontological Society of America. This annual award recognizes outstanding early career contributions to the field. Levy's research focuses on psychosocial influences on aging.

Robert W. Makuch, PH.D., professor and former head of the Division of Biostatistics in the School of Public Health, was named a fellow of the American Statistical Association in June. Makuch was honored for his statistical consultations to government and the pharmaceutical industry, for his contributions to the design and analysis of clinical trials and for his administration of an academic biostatistics division.

SEND FACULTY NEWS TO
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 06519-0612, or via e-mail
 to claire.bessinger@yale.edu

The bigger questions in science

For a whopping 360 students, bioethics course tackles problems at “the core of our existence.”

By Cathy Shufro

When Political Science 309b — “Leading Issues in Bioethics”—met for the first time a year ago, Arthur W. Galston, P.H.D., the Eaton Professor Emeritus of Botany and lecturer in political science, expected that the 125-seat Mason Laboratory would be the right size for the undergraduate course. But on Day One students were “hanging from the rafters,” said Galston. The class moved to the 250-seat auditorium in the Whitney Humanities Center, but even there, a hundred students were left standing in the aisles. The course had to move again, this time to the cavernous law school auditorium. Class size: 360 students, making Poli Sci 309b one of the largest courses offered at Yale College last spring.

Although Galston was surprised by the huge turnout, he’d known that there was “pent-up demand” for a course in bioethics, the study of the ethical consequences of advances in biology. For 12 years, he had turned away 60 students each time he’d offered a bioethics seminar that was limited to 18.

“These are human interest problems. They get to the very core of our

“Syllabus” is an occasional feature in Yale Medicine profiling courses of special interest at the School of Medicine and throughout the university.

existence,” said Galston, a member of the Institution for Social and Policy Studies. Galston assembled his course by calling in experts from every corner of campus—from the law school to the divinity school, from forestry to genetics—and including what he called “the superstars from the medical school.” They gave 26 lectures on topics ranging from the ethics of stem cell research, to the Judeo-Christian attitude toward nature, to why Jehovah’s Witnesses seek the right to deny blood transfusions to their children.

“You have some large questions,” said Galston. “Is it fair that Mickey Mantle got a liver when he ruined his liver through excessive alcohol? Does nature have intrinsic value? Does it matter if a species goes extinct?”

“The best thing about the course was all the different voices we heard,” said Robert Fisher, a divinity school student who has worked as a hospital

chaplain. Among the voices were those of Kenneth K. Kidd, P.H.D., professor of genetics, who discussed ownership of the human genome sequence and whether, from a geneticist’s perspective, race exists; author Sherwin B. Nuland, M.D. ’55, HS ’61, clinical professor of surgery, talking about the end of life; and Marc I. Lorber, M.D., professor of transplant surgery, on the ethics of obtaining organs for transplantation. Other speakers discussed topics ranging from world population growth to the potential hazards of genetically modified foods.

Suzana Zorca, a Yale College senior last spring who is now attending medical school, said the course complemented her biotechnology course. “You can’t help but be in [biotech] class and think of the ethical controversies that must be raging around these issues.”

“The course attracted people of literally every conceivable major,” said



TERRY DAGRADI

An undergraduate course in bioethics has become one of the most popular classes at Yale.

Andrew J. Read, a biology major. (The course is cross-listed as Molecular, Cellular, and Developmental Biology 130b.) Although Read said that in some courses discussion sections can be tedious, the give-and-take was lively in his bioethics section, led by genetics doctoral student Stacey Thompson. “People were very much awake, with the discussions becoming so heated that we almost didn’t want to leave when the buzzer signaled the end. ... I found myself re-evaluating some of my own opinions on the subjects, with the realization that most ethical dilemmas have no clear-cut answers.”

Galston’s interest in bioethics dates to the mid-1960s, when a chemical

he’d developed to improve soybean production was combined with another and used as a defoliant in the Vietnam War. Galston was alarmed: the defoliant, the infamous Agent Orange, could cause birth defects. He and some colleagues eventually managed to convince President Richard Nixon to suspend the use of Agent Orange. “This is what catapulted me into activism and started me into bioethics,” said Galston.

The course was offered again this spring, and this time Galston reserved a large auditorium.

Reading list: Poli Sci 309B/MCDB 130B

Students taking the course bought three textbooks: *Ethical Issues in Modern Medicine*, sixth edition, edited by Bonnie Steinbock, John D. Arras and Alex John London (McGraw-Hill); *Environmental Ethics: Readings in Theory and Application*, third edition, edited by Louis P. Pojman (Wadsworth); and *The Human Embryonic Stem Cell Debate: Science, Ethics, and Public Policy*, edited by Suzanne Holland, Karen Lebacqz and Laurie Zoloth (MIT Press). Students also read “The Oath of Hippocrates” and articles including “Dying Words” by Jerome E. Groopman (*The New Yorker*, Oct. 28, 2002); “Financial Compensation for Cadaver Organ Donation: Good Idea or Anathema,” by A.L. Caplan, C.T. Van Buren and N.L. Tilney (*Transplantation Proceedings*, Vol. 25, No. 4, 1993); and “Psst! Sell Your Kidney?” by Nicholas D. Kristof (*The New York Times*, Nov. 12, 2002).

A week of fund-raising nets \$20,000 for the hungry and homeless

Thursday usually finds Interim Dean Dennis D. Spencer, M.D., HS ’77, in the operating room. But last November 20, he was on the stage in Harkness Auditorium, trying to raise money for the 11th annual Hunger and Homelessness Auction.

“I grew up on a farm,” he said. “I’m used to auctioning off cattle. We started at \$2,000.”

Rather than cattle on the block that day, bidders could vie for weeklong stays at Vermont ski condos, dinners with deans, afternoon sloop sails in New Haven Harbor, or airplane rides over Connecticut.

Among the more offbeat items this year were break dance lessons by second-year student Edward Teng and a polar bear swim offered by second-year student Duncan Smith-Rohrberg, who agreed to plunge into the bidder’s choice of body of water and stay in for five minutes plus another minute for each \$2 donated—to a maximum of \$20. A group of his classmates offered \$100 if he went in naked.

The auction has expanded over the years. What was once concentrated in a rowdy two hours in the auditorium now takes place over a week and includes several new events. First- and second-years hold a fund-raising football game on Harkness Lawn; there’s a “hunger banquet” to introduce people to the world of the food-deprived; a party at the weekly “Club Med” gathering in Harkness Dormitory benefits the auction fund; and for three days preceding the live auction there’s a silent auction in the Sterling Hall of Medicine.

This year’s auction netted more than \$20,000, which will go to Loaves and Fishes, LifeHaven, Youth Continuum, New Haven Home Recovery, Community Health Care Van, Downtown Evening Soup Kitchen and St. Thomas More, the Chapel and Catholic Center at Yale.

—John Curtis



TERRY DAGRADI

Arthur Galston led a fall course on issues in bioethics that ranged from the ethics of stem cell research to the Judeo-Christian attitude toward nature.

Art class gives students of medicine, anatomy another resource to draw upon

On occasional Thursday afternoons throughout the academic year's first semester, students returned after hours to the gross anatomy lab armed not with scalpels, but with brushes, paints, sketch pads and cameras. There, Mark R. Depman, M.D., a clinical instructor in medicine who works part time in the emergency room at Lawrence & Memorial Hospital in New London and spends part of each week in his Fair Haven art studio, encouraged the students to examine the human body with an artist's eye. This was not a drawing class—he offered no instruction on the fine points of charcoal or watercolors. Students could, he said, “use drawing and photography as a tool to stop and look again” at the human body.

Erin Kiehna, a second-year student, said the art class gave her a renewed appreciation for not only the body but the spirit that once occupied it. “It’s nice to sit in silence with a sketch pad in hand and really appreciate the donor,” she said. In anatomy class, she added, “You feel like you’re ransacking it, as you try to find everything.”

Depman, a member of the arts subcommittee of the Program for Humanities in Medicine, proposed the elective course last year and opened it to students at all levels of study. “I am hoping that over the coming year,” Depman said, “students will use this as an opportunity to look at the history of how we examine the body and how technology has changed the learning process.”

Although he started painting with oils and watercolors in his youth, Depman now creates images on film. (Depman’s latest work, two series of Cibachrome photographs and one of digital photographs, opened at the Nancy Hoffman Gallery in Manhattan’s Soho district in December.)

In the Thursday afternoon art class, students cluster around a cadaver or

skeleton and draw with charcoals, paint with watercolors or set up cameras as they pursue an image. They come to the class with a mix of goals.

“After you’ve gone through the wards and spent time with patients you’re able to look at anatomy in a different way,” said Vernee Belcher, a fourth-year student who found the course an artistic way to become reacquainted with the human body two years after taking the gross anatomy class. Said Tina Dasgupta, in her third year of the M.D./PH.D. program, “Every patient has a story. There is something more to a patient than a chief complaint and history of present illness.” She also found the course a way to take a fresh look at the human body. “Form meets function in a fantastic way.”

Depman, a Cornell medical graduate who studied drawing at Oxford, is fine-tuning the course and, sometime in the future, may also teach technical skills. For now, though, he’s satisfied to let students pursue their own ideas.

“It is a very important message for the medical school to put out there—that this is available and it can help you mature as a health care professional and a human being who practices medicine,” he said. “There is such a danger of losing the human impetus and human contact in practicing medicine.”

—J.C.



TERRY DAGRADI (2)



TOP Natasha Archer, one of the emcees from the second-year class, urged students and faculty to spend money at the Hunger and Homelessness Auction in November.

ABOVE Interim Dean Dennis Spencer enjoyed his debut as an auctioneer at the annual event.



JOYCE KAUFMAN

Joyce Kaufman, a second-year student, chose photography as her medium for the study of the skeleton.



MARTIN KLIMEK

As chief of California's Division of Chronic Disease and Injury Control, Donald Lyman has successfully campaigned to reduce tobacco use. His next target is obesity.

Speaking the language of prevention

Building on success with smoking, California's top public health official turns state's attention to obesity.

When **Donald O. Lyman**, M.D. '68, oversees a media blitz against smoking in California, he draws upon his training in medicine, his years in public health and his knowledge of the differences between Spanish dialects. In California, you have to know whom you're talking to: an anti-smoking ad in the dialect spoken in El Salvador won't go over big with Mexican-Americans. And vice versa.

Lyman picked up a sensitivity to linguistics along the way as chief of the Division of Chronic Disease and Injury Control, a post that his colleagues say is California's equivalent of surgeon general. "California has become to this nation what New York was a century ago. It's the port of entry to immigrants," says Lyman. "You drive down the street in LA with the windows open and smell the wonderful smells that change from block to block." He describes the state's 36 million residents as "a wonderful collection of well-motivated people who came here looking for a better life." Helping to provide that life is Lyman's mission as the state's highest-ranking civil service physician. Under Arnold Schwarzenegger, he's serving his fifth governor since taking the job in 1978. This year he heads a staff of 375 employees and oversees a \$200 million budget.

His agency's biggest victory has been its anti-smoking campaign, which

reduced cigarette consumption in California by 64 percent between 1988 and 2003, based on cigarette sales, according to California and federal data. (During the same period, consumption fell 36 percent nationwide, excluding California.) "It's huge," says Lyman. A 2000 analysis in *The New England Journal of Medicine* found that California's anti-smoking program resulted in 33,300 fewer deaths from heart disease between 1989 and 1997 than would otherwise have been expected.

That \$1 billion program was funded by California's Proposition 99, a 1988 law that increased the cigarette sales tax to fund the nation's largest-ever tobacco control program. Lyman claims its success cost the tobacco industry \$2.9 billion in California sales in the decade beginning in 1989, and he cheerfully reports that the industry views California as "Public Enemy Number One, with a well-funded program that works."

How did they do it? As in all public health campaigns, from promoting seat belts to discouraging teen drinking, they did it partly by changing society's "ethos." They challenged the assumption that smoking is a neutral, strictly personal choice, both "from the top down," with anti-smoking billboards and public service announcements, and also from the ground up, by approaching community groups and civic leaders. This grass-roots strategy aimed to get communities to adopt the battle against smoking as their own. The Division of Chronic Disease and Injury Control hired public health educators to visit neighborhood groups, schools, city councils and workplaces to discuss how smoking contributes to disease.

Lyman explains that although public service announcements and educational campaigns have clearly conveyed the dangers of smoking, “very few people come together and sit down and talk about smoking. ...When you actually sit down and look someone in the eye and ask, ‘What can we do about this?’ you’re likely to get a response.” Billboards and other anti-smoking ads make people receptive, but “you’ve got to engage people personally. That’s the key to the program.” That process would be called “community norm change” by liberals or “social engineering” by conservatives, “but ... it’s all the same,” says Lyman. The health educators introduce a shift in perspective by explaining how tobacco companies cynically target vulnerable preteens and young teens. “The smoker is no longer portrayed as the villain,” says Lyman. “The smoker’s the victim.”

Lyman is unperturbed by Gov. Schwarzenegger’s penchant for cigars. “I worked with him when he was our chair of the Governor’s Council on Physical Fitness and Sports, and he was consistently supportive of all the ‘health stuff’ we did,” recalls Lyman. “The other council members ribbed him about the cigars, and he was appropriately sheepish in reply.”

Young people have proven the most resistant to anti-smoking efforts, and Lyman credits tobacco industry advertising with creating “the Joe Camel generation,” in which nationally one in four 18- to 25-year-olds smokes. But the end result—which is the point for a utilitarian like Lyman—is that smoking among California adults dropped from 23 percent to 17 percent between 1985 and 2002, and the California

rates among teens are now among the lowest in the nation. Lyman’s department kept track of smoking rates using a series of surveys overseen by the University of California, San Diego.

The American Cancer Society’s California division, of which Lyman is the current president, reported that the state lung cancer rate dropped 14 percent from 1988 to 1997, based on the records of the state’s cancer registries. That compares to declines of 2 to 3 percent nationally, according to data collected by the National Cancer Institute. “To see the lung cancer rates go down is really quite amazing,” says Diane J. Fink, M.D., medical director of the California cancer society. “Don’s leadership has been paramount.”

His agency’s biggest failure? “We’ve been doing a miserable job on nutrition and physical activity,” he says. Like smoking, says Lyman, obesity, bad food choices and sloth all contribute to cancer and cardiovascular disease, which account for two-thirds of deaths and illnesses in the state. “We have an epidemic of obesity and a startling lack of physical activity,” says Lyman. Lyman said the adult obesity rate in the state (a body mass index of 30 or more indicates obesity) rose from 10.6 percent in 1991 to 18.9 percent in 2000, and type 2 diabetes in children is burgeoning.

Lyman says his agency is using the same “sandwich approach” (a low-fat sandwich, no doubt) that it used successfully against smoking: pairing a top-down media campaign with a foundation of grass-roots policy changes. In the policy realm, the mammoth Los Angeles school district voted in 2002 to ban soft drink sales to its

748,000 students by this year. Sensitive planning, like linking bicycle trails to subway lines, can make exercise more convenient. Messages to eat well derive in part from the state’s huge agriculture industry and its grocery store chains, which push produce with the catch phrase “five a day.”

As for Lyman himself, living a busy life that includes a third of his time on the road, he manages to eat “four or four and a half” of the five recommended daily servings of fruits and vegetables and to fit in an hour of combined aerobics and weight training five days per week. He and his wife, Elisabeth Blakeslee Hall Lyman (who also works in public health, as California’s assistant administrator for health services for children), both have centuries-old ties to Connecticut, including to Connecticut’s well-known Lyman Orchards. Elisabeth spent her childhood in South Hadley, Mass., down the street from the Giamattis, whose son grew up to be president of Yale. Despite Yankee roots, the Lymans and their two children consider themselves Californians.

Lyman finds inspiration by viewing his job as the promotion of social justice. He is fond of an aphorism from the *Talmud* that he remembers hearing in a speech by former Yale President A. Bartlett Giamatti: “You are not required to complete the work, but neither are you free to desist from it.”

—Cathy Shufro



BOSTON RED SOX

For another public health trailblazer, a tobacco control milestone in the Bay State

Howard K. Koh, M.D. '77, M.P.H., is another Yale medical alumnus who has won a major battle in the tobacco wars as a top state health official. When asked to name the most memorable moment in his five-and-a-half-year stint as Massachusetts commissioner of public health, Koh barely hesitates. "I'll never forget pulling down the last tobacco billboard in Massachusetts with the attorney general, Tom Reilly," Koh says. "That was a very public, concrete example of how much progress we had made."

Koh's experience as a clinician (he's board-certified in internal medicine, hematology, medical oncology and dermatology) inspired him to join Massachusetts' fledgling anti-tobacco campaign in 1992 as a volunteer for the American

Cancer Society and the Massachusetts Coalition for a Healthy Future. "I saw for myself what happens when prevention isn't addressed or is overlooked, particularly with respect to cancer," he says. During his watch as commissioner, he saw the state's aggressive efforts pay off: Massachusetts reported the fastest decline in cigarette smoking in the nation—adult cigarette consumption dropped 4 percent per year while most states saw a 1 percent annual decline. "People said the industry was too strong and the addiction was too strong, and it was impossible to make a difference," Koh says. "We showed that we could change the social norm and prevent addiction, especially for kids."

For Koh, who left his post in January 2003 to become professor and associate dean for public health practice at the Harvard School of Public Health, the victories in the tobacco wars are part of a larger legacy. "Just before I stepped down, a national report ranked Massachusetts as the third healthiest state in the country," Koh recalls. "We had risen from number 10. It was a tremendous honor to be commissioner and see that level of progress being made."

However, the events of September 11, 2001, presented Koh and other state public health officials with an unexpected and daunting set of challenges; foremost among his goals at Harvard is to prepare students to grapple with bioterrorism and other 21st-century hazards. "The essence of public health is protecting people from threats and preventing suffering," he says. "In the post-9/11 age, public health has been broadened dramatically in its scope, and we have a critical function."

Howard Koh, former commissioner of public health for Massachusetts, saw tobacco use decline dramatically in his state. He also had the chance to throw out the first pitch at a Red Sox game at Fenway. Koh now teaches public health and is an associate dean at Harvard.

Accomplishment and a dedication to public service run in Koh's family, along with strong ties to Yale. Koh's brother, Harold H. Koh, J.D., a renowned expert on human rights, was recently named dean of the law school, where his sister, Jean Koh Peters, J.D., is a clinical professor. Koh's mother, Hesung Chun Koh, Ph.D., one of the world's leading East Asian scholars, retains an emeritus appointment at Yale. She and her late husband, Kwang Lim Koh, Ph.D., a lawyer and democracy activist, founded in 1952 what is now known as the East Rock Institute, the oldest Korean cultural institute in the United States. (Howard and Harold Koh and their parents have been named to the K100, a list of 100 leading Koreans and Korean-Americans in the first century of Korean immigration to the United States.) Koh says his parents were an inspiration to all of their children. "Both of them viewed life in a very broad, societal way, if not a global way," he says. "When people ask where this commitment to serve came from, I tell them—it's in my blood."

For his Boston-area neighbors, though, one honor among the many listed on Koh's CV surely arouses the greatest envy. After being named a "Medical All-Star" by the Boston Red Sox for his work on melanoma, Koh, with his wife and three children standing by, threw the first pitch in a game at Fenway Park last May. "That," Koh says, "was a magical public health experience."

—Peter Farley

Roaming the world's hot spots, ensuring that care reaches those who need it

Almost two decades after completing his residency in internal medicine at Yale, **Michael V. Viola**, M.D., HS '66, was doing the kinds of things that serious-minded doctors do: treating patients, teaching students, heading the cancer center at the State University of New York at Stony Brook. But then something happened to alter his sure-footed career path.

While he was at Stony Brook in the early 1980s, a large influx of Salvadorans and Guatemalans arrived to escape homelands rocked by civil wars. "It was an extraordinarily unfortunate situation," recalls Viola, who received his medical degree from McGill in 1964. "Most of them were illegal, and they had no health care. They weren't designated as refugees escaping an oppressive government, because the United States was supporting their governments."

Viola started collecting and sending medicine to villages in El Salvador. As that effort grew, he was joined by other doctors, and a small nongovernment relief organization was born. The group crystallized into Medicine for Peace, with Viola as its founder and director. He continues to direct the group from his home in the Washington area.

Today, Medicine for Peace, an all-volunteer organization run by a five-member executive board, has about 50 affiliated physicians and nurses from around the country. During and after the first Gulf War, members of the group spent five years in Iraq, filming the destruction, teaching Iraqi physi-

cians, studying children's nutritional needs and delivering medicine. In 1993, members helped negotiate the release of American oil executive Ken Beaty, who was arrested by Iraqis after he strayed across the border from Kuwait. The group's involvement in the rescue put an end to their efforts in Iraq.

"Once that happened, the Iraqis never quite looked at us the same way again," Viola said. "We'd done a lot of work with children, so they kind of trusted us. But once we were critical of their government, and it looked like we were working with the U.S. government, things changed, and we were kicked out in 1995."

While Medicine for Peace maintains a presence in Haiti and Bosnia, its involvement in the current war in Iraq has been minimal because of the danger and restricted access. "There's not much we can do," Viola said. "We were told we need to have armed escorts at all times. We can't operate like that." The group hopes to send a team to Baghdad "to locate a large group of Iraqi children we brought to the U.S. for surgery in the 1990s. We hope they have survived all of the violence."

Unlike larger, better-known relief organizations, such as Doctors without Borders, Medicine for Peace (www.medpeace.org) won't take government funding (it relies on private donations) and will criticize U.S. policy. "We're smaller and more freewheeling," Viola said. "We tend to go to controversial places and take controversial stands." But that renegade approach has risks. Noting that by the end of 2003, 57 relief and diplomatic workers had been killed since the current Iraq war began in March 2003, Viola said, "Humanitar-

Michael Viola traveled to Iraq in the 1990s, where the organization he leads, Medicine for Peace, trained Iraqi physicians, delivered medicine and studied children's nutritional needs.



DOUG HOSTETTER

ian workers used to be protected, but the nature of war has changed. Now civilians are targeted. If belligerents kill civilians, they certainly don't mind killing relief workers." In August a bomb at United Nations headquarters in Baghdad killed 17 people.

Still, despite the danger, Viola, who runs the U.S. Department of Energy's Medical Sciences Division, spends as much time as possible working for Medicine for Peace. "I'm not saying you get an enormous reward. There's nothing rewarding about mass graves or large numbers of children dying of starvation, but you realize you're having an impact in some small way."

—Jennifer Kaylin

Familiar Faces

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



John Baxter



Shelley Taylor



Robert Frelick and Jane Frelick



Eva Henriksen



Robert Higgins



Liselotte Pieroth-Vinals and Antonio Vinals

Three Yale alumni elected to Institute of Medicine

Three Yale alumni were among 65 new members elected to the Institute of Medicine in October. They are **JOHN D. BAXTER, M.D. '66**, professor of medicine in the Department of Medicine and Diabetes Center, University of California, San Francisco; **DOUGLAS R. LOWY, M.D., HS '75**, chief of the Laboratory of Cellular Oncology and deputy director of the division of basic sciences and Center for Cancer Research, at the National Cancer Institute; and **SHELLEY E. TAYLOR, PH.D. '72**, professor of psychology at the University of California, Los Angeles.

Baxter uses the tools of structural and molecular biology to determine the workings of nuclear receptors in health and disease and to design ligands with selective actions on nuclear receptors. Lowy studies the molecular biology of tumor viruses, oncogenes and tumor genes. Taylor's research explores the interaction of biology and behavior as they affect mental and physical health.

1940s

Robert W. Frelick, M.D. '44, of Wilmington, Del., liaison to the National Cancer Advisory Board for the Association of Community Cancer Centers, received the Christiana Care Health System's annual commendation for excellence in October. The award recognizes a current or former member of the medical-dental staff of Christiana, Delaware's largest health care provider, for outstanding clinical care and compassion and for distinguished achievement in education,

research, community service or leadership. Frelick, a medical oncologist since the specialty's earliest days, was honored for more than five decades of service and leadership. Frelick and his wife, Jane, met while he was in medical school and she was a nursing student at Yale.

Robert H. Furman, M.D. '43, FW '45, writes to say: "We're enjoying retirement at La Posada, a continuing care retirement community in Green Valley, Ariz." Furman attends a medical journal club and weekly grand rounds at the University of Arizona School of Medicine. He also participates in a weekly lecture series called "The Forum at La Posada."

Roslyn L. MacNish, M.P.H. '41, of Wethersfield, Conn., is retired and enjoying photography and attending camera clubs and councils. During her career MacNish was a statistician in public health at the Hartford Hospital Tumor Clinic and for the state of Connecticut's tuberculosis control program.

1950s

Eva Henriksen, M.D. '54, writes to say that "in Los Angeles, I quilt, visit with daughter Liz and granddaughters Ryann, 8, and Addison, 5, and e-mail daughter Mary, who with husband Reggis has been in South Africa, Thailand and Australia as part of an around-the-world tour. I do anesthesia consultations on operating room-related deaths for the LA coroner's office."

1960s

Robert L. Johnson, M.D., HS '64, clinical professor of otolaryngol-

ogy at the University of California, San Francisco, for more than 30 years, writes to say that "almost 40 years have passed since I was an otolaryngology resident at Yale. Married for 42 years to Barbara, a staff pediatric nurse, with three adult children all living in the Bay area. My younger daughter recently received her doctorate in psychology. My wife and I returned from Thailand, Bhutan and Laos, where I gave lectures on sinusitis."

1970s

Ian B. Berger, M.D., M.P.H. '74, is president of Houston-based InFOCUS, a nonprofit organization promoting eye care for all, and director of the InFOCUS Center for Primary Eye Care Development, whose domestic programs in poor and rural areas provide eye care for migrant farm workers, Native Americans and other populations in need. InFOCUS has promoted a new paradigm, the Vision Station, to deliver primary eye care. Berger, with colleague Larry Spitzberg, PH.D., O.D., has also created the Focometer, a hand-held refracting instrument that measures visual errors and determines prescriptions. It was designed for use in remote or poor areas and is used in 40 countries.

1980s

Robert S.D. Higgins, M.D. '85, the Mary and John Bent Chair of Cardiovascular-Thoracic Surgery at Rush-Presbyterian-St. Luke's Medical Center, was honored as a leader in public health and medicine by the Gift of Hope Organ & Tissue Donor Network and its African American Task Force at a ceremony in Chicago

in November. Higgins was honored for establishing a standard of excellence, improving the health of communities and supporting efforts to save and improve lives through organ and tissue donation.

Marie (Ciaccio) Tsivitis, M.P.H. '86, staff associate at the Long Island State Veterans Home in Stony Brook, N.Y., is teaching a new course titled "Issues in Public Health" at Stony Brook University as an adjunct staff associate in infection control. Tsivitis also writes that she and her husband have two children, Alexandra, 8, and Christopher, 4.

1990s

Antonio F. Vinals, M.D. '93, writes to say that he and his wife, Liselotte Pieroth-Vinals, M.D., are enjoying living in Manhattan. Vinals is an ophthalmologist at the Manhattan Eye, Ear and Throat Hospital. He and Pieroth met at Yale in 1992. She was a visiting international medical student and intern at Yale and completed her ophthalmology training at Columbia University and a fellowship in oculoplastic surgery at the New York Eye and Ear Infirmary, where she is now on the staff. They are the proud parents of Matilde Beatrix, who was born at Columbia-Presbyterian Hospital on December 12 and weighed seven pounds.

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

VISIT US ON THE WEB info.med.yale.edu/yymm

Robert L. Arnstein, M.D., of Hamden, Conn., whose career as a psychiatrist at Yale spanned almost 40 years, died on October 27 at the age of 84. For three decades, Arnstein was the chief psychiatrist at Yale University Health Services. Under his guidance, Yale became a national model for campus mental health programs. In 1971 he became a clinical professor of psychiatry at the School of Medicine. He retired in 1989.

Robert F. Bradley, M.D. '43, former medical director and president of Joslin Diabetes Center in Boston, died on October 12. He was 83. As president of Joslin from 1977 to 1987, he oversaw the center's expansion and championed the use of oral agents for treating type 2 diabetes. A 1941 Yale College graduate, Bradley served in the Navy after graduating from the School of Medicine and trained at the Lahey Clinic, New England Deaconess Hospital and Joslin Clinic. He served as editor of *Joslin's Diabetes Mellitus* and as an expert witness in the Claus von Bulow murder retrial in 1985.

Mary E. Ellis, M.P.H. '48, of Decatur, Ga., died on September 27 at the age of 81. Ellis was a teacher at the McLendon Elementary School in DeKalb County, Georgia, for more than 20 years. She taught church school for more than 50 years and wrote a Christian education curriculum for the Presbyterian Church.

Knox H. Finley, M.D. '30, of San Francisco, died on September 15 at the age of 99. After graduation from medical school Finley completed a fellowship in neurology at the Kaiser Wilhelm

Institute in Germany and was subsequently board-certified in neurology and psychiatry. He practiced medicine for 45 years at the California Pacific Medical Center in San Francisco.

Julian Frieden, M.D. '48, of White Plains, N.Y., a cardiologist associated with Montefiore and New Rochelle hospitals, died on September 29 of Parkinson's disease. He was 78. Frieden published pioneering articles on peritoneal dialysis, the measurement of intracardiac pressure, the use of lidocaine to stabilize heart rhythm and the role of salt in hypertension.

Nancy G. Hildreth, M.P.H. '78, M.P.H. '79, PH.D. '81, of Rochester, N.Y., died on September 30 after an eight-year battle with amyloidosis. She was 54. Hildreth was an assistant professor of epidemiology at the University of Rochester.

Barry M. Kacinski, M.D. '80, PH.D. '81, HS '83, a professor in the departments of therapeutic radiology, dermatology, and obstetrics and gynecology, died on November 20 following a heart attack. He was 50. Kacinski led groundbreaking research to define the effects of growth factors and oncogenes in the development of malignancies. He had an international reputation for his contributions to the field of DNA repair and to the understanding of dermatologic and gynecologic malignancies.

Lawrence K. Pickett Sr., M.D. '44, of Ithaca, N.Y., died on November 15 at the age of 84. Pickett was the first pediatric surgeon in the Syracuse area, where he practiced from 1950 to 1964. In 1964

he came to Yale-New Haven Hospital to establish a pediatric surgical department. At Yale he was named the William H. Carmalt Professor of Clinical Surgery and Pediatrics. He also served as associate dean of clinical affairs and chief of staff of the hospital. He retired in 1983.

Fredrick C. Redlich, M.D., former dean of the School of Medicine and a founding figure in the field of social psychiatry, died on January 1 of congestive heart failure. He was 93.

Redlich, who was born in Vienna, came to Yale in 1942 for the start of a career that lasted more than 30 years. He served 17 years as chair of the Department of Psychiatry and five years as dean of the medical school. While chair of psychiatry he was credited with transforming a foundering department into one that promoted psychiatry based on a mix of basic research, clinical work and behavioral science. As one of the earliest practitioners of social psychiatry, he studied links between mental illness and social milieu. He was co-author of nearly 100 scientific papers and six books, including one he called a "pathography" of Hitler's mental state.

Robert H. Stevens, M.D. '36, died on November 30 at Yale-New Haven Hospital. He was 96. During World War II Stevens served in the Army, in France and Germany, as a neurosurgeon. He practiced neurosurgery in Utica, N.Y., for 50 years.

Max Taffel, M.D. '31, of Barre, Vt., died on September 19 at Yale-New Haven Hospital. He was 94. Taffel, a neurosurgeon, was on the Yale-New Haven Hospital

staff for 46 years. During the Iwo Jima and Okinawa campaigns in World War II he was the only neurosurgeon on the island of Saipan, where he earned a Bronze Star Medal. His goals were to be "an honest surgeon and devoted father, to instill the love of learning into the hearts and minds of young people ... and to do harm to no one."

Joseph B. Warshaw, M.D., former deputy dean for clinical affairs and chair of pediatrics at the School of Medicine, died on December 29 from multiple myeloma. Warshaw was 67 and "an expert on fetal growth and neonatal medical care who advanced the understanding of the way organs mature in normal and diabetic pregnancies," according to his obituary in *The New York Times*. For the past three years Warshaw had served as dean of the University of Vermont College of Medicine. Among his accomplishments there was the launching of an M.D./PH.D. program. Warshaw was honored last March at the School of Medicine at the second "Joseph B. Warshaw Symposium on Developmental Biology."

SEND OBITUARY NOTICES TO
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Running for governor, again

Throughout his eight years as governor of Puerto Rico, Pedro J. Rosselló, M.D. '70, M.P.H., concerned himself with two main issues—universal health care and statehood for the island. He succeeded in one with a reform that brought health insurance to all, yet victory narrowly eluded him in the other. In two non-binding plebiscites, voters expressed a preference for commonwealth status.

In 2000, at the end of his tenure, Rosselló chose not to seek a third term. Instead he went to Washington to teach public health at George Washington University and analyze disenfranchisement and universal health care at the Woodrow Wilson International Center for Scholars. Early in 2003 Rosselló announced his return to politics, and in November he won the pro-statehood New Progressive Party's primary with 76 percent of the vote. This fall he will face two candidates in the governor's race.

Rosselló, who trained and practiced as a pediatric surgeon after earning his Yale medical degree, comes to his third race with a mixed legacy. In his previous terms he replaced state-run hospitals and clinics with an insurance program that increased access to health care for the poor ["A New Prescription for Puerto Rico," Winter 1999]. His health care reform had its critics—including physicians who found the capitated payments too low. Nevertheless, by 2001 more than 1.8 million of an estimated 2.1 million potential clients were enrolled in the ongoing program.

Despite his vigorous campaigns for statehood—which he believes will spur trade and investments on the island—Puerto Ricans have voted to maintain commonwealth status. And allegations of corruption in his administration have dogged him since he left the governor's office.

Rosselló has not been implicated in any wrongdoing, but his former education secretary and the president of the island's Chamber of Commerce were arrested in an investigation of a kickback scheme. Another executive was convicted of extorting payoffs from contractors who wanted access to cabinet members. "I know I acted in good faith at all times, not only legally, but ethically and morally," Rosselló said in a radio interview before the primary. He has pledged to crack down on corruption, if elected. He has also vowed to seek another referendum on the question of statehood.

—John Curtis



OCTOBER 1953 Alumni Bulletin

"General plans for the construction of the new Edward S. Harkness Memorial Residence Hall, generous gift of the Commonwealth Fund, have been completed as the result of several meetings of the Building Committee with the architects, Douglas Orr of New Haven and Guglar, Kimball & Husted of New York. ... It is hoped that ground can be broken early in 1954 and that the new quarters for Yale medical students can be finished and equipped for occupancy in September 1955. ...

"One wing, of eleven stories and ground floor, will provide 219 single rooms for male students, as well as ten suites for students or graduate advisors. The other wing, four stories high, will contain thirty-five small apartments. The latter will be occupied by pairs of single women students and by a few married medical students and their wives. The single rooms will include lavatories and built-in closets. Shower rooms will be provided on each floor. The apartments will consist of a living room, bedroom, bath, and kitchenette unit. The apartment wing will have its own entrance and will also communicate with the main lounge. Each wing will have its own automatic elevators. Other living quarters will include a large apartment for a resident manager and his family and a living room-bedroom-bath combination for the accommodation of visiting lecturers and other guests of the school. ...

"Comfort and convenience have been emphasized. ... The completion of the new residence hall should increase significantly the efficiency and well being of the able group of young men and women studying at the School of Medicine."



FALL/WINTER 1983 Yale Medicine

"The John B. Pierce Foundation Laboratory celebrated its 50th anniversary on November 4th, and paid tribute to Dr. A. Pharo Gagge, fellow emeritus. Dr. Gagge has been a member of the Laboratory's scientific staff since it was founded in 1933 to conduct research and educational programs 'for the increase of knowledge to the end that the general hygiene and comfort of human beings and their habitations may be advanced.'

"Dr. C.E.-A. Winslow was appointed the first director of the Laboratory while he was chairman of the Yale Department of Public Health, and he retained both offices until his retirement in 1945. Under his leadership, and that of subsequent directors, the Laboratory has gained worldwide recognition for its many significant contributions to the field of environmental physiology. In recent years of energy shortages and increasing pollution production, their work has assumed added importance as governments seek a balance between energy conservation and a healthful environment.

"The close relationship between the Pierce Laboratory and the Department of Epidemiology and Public Health has continued. ..."

The first part of the document discusses the importance of maintaining accurate records of all transactions. It emphasizes that every entry, no matter how small, should be recorded to ensure the integrity of the financial data. This includes not only sales and purchases but also expenses, income, and any other financial activities. The text explains that proper record-keeping is essential for identifying trends, managing cash flow, and preparing for tax obligations. It also highlights the role of these records in providing a clear audit trail, which is crucial for both internal management and external audits.

The second section focuses on the classification of expenses. It details how different types of costs should be categorized to facilitate better financial analysis. For example, it distinguishes between fixed and variable costs, as well as direct and indirect expenses. The text provides examples of how to allocate shared costs and discusses the impact of these classifications on profit margins and budgeting. It also touches upon the importance of regular reviews to ensure that the classification system remains relevant and accurate over time.

The third part of the document addresses the issue of budgeting and financial forecasting. It outlines the steps involved in creating a realistic budget, from identifying goals and objectives to allocating resources and monitoring performance. The text discusses various forecasting techniques, such as trend analysis and ratio analysis, and provides guidance on how to use these tools to make informed decisions. It also emphasizes the need for flexibility in the budgeting process, as circumstances can change, and adjustments may be necessary to stay on track.

The final section discusses the importance of transparency and communication in financial management. It stresses that clear and concise reporting is essential for building trust and ensuring that all stakeholders have a good understanding of the organization's financial health. The text provides tips on how to present financial data effectively, including the use of charts, graphs, and tables to make complex information more accessible. It also discusses the importance of regular communication and collaboration between different departments to ensure that financial goals are aligned with overall business objectives.

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