

Yale Medicine

YALE UNIVERSITY SCHOOL OF MEDICINE
SPRING 2000



a bug's life (cycle)

How vector biology is changing public health

On the cover

With the arrival of spring—and the reappearance of mosquitoes—New York City is bracing for the possible recurrence of West Nile fever, a virus not seen in the Western Hemisphere before 1999. Investigators believe the mosquito species *Culex pipiens* (cover) is the most likely vector of the disease, which killed seven people at the end of last summer and may have crossed the Atlantic in birds. At Yale, a molecular approach to vector-borne illnesses promises to reveal new targets for intervention. Page 16.

This page: The protozoan responsible for malaria, which kills two million people each year.

COVER: THE BRITISH MUSEUM THIS PAGE: SERAP AKSOY

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Eight decades of the Yale System

As the school takes an exceptionally thorough look at both how and what it teaches, we invited alumni to reminisce about the Yale System of their day.

LETTERS

Another side of Bob Gifford

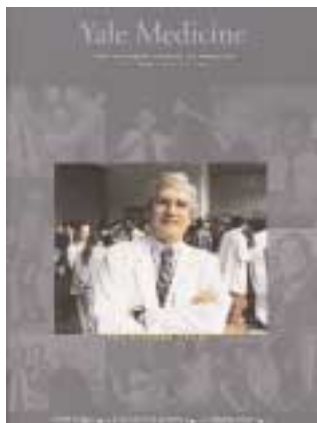
To the Editor:

John Curtis' article on Robert Gifford ["Goodbye, Dr. Gifford," Fall 1999/Winter 2000] captures many of my best memories of Yale. Like many others, I was fortunate enough to have Bob Gifford as a mentor during my first two years of medical school. He made the transition into medicine so fascinating and inspiring for us that it was no coincidence that my med school chum Jim Sullivan, M.D. '73, and I became rheumatologists.

The only other teacher-physician who made a deep impression on me was the late infectious disease specialist and chief of medicine at Waterbury Hospital, George Thornton, M.D. Oddly enough, he grew up with Bob and went to church where Bob's father was the minister. Dr. Thornton related to me (and many others, I'm sure) that Bob was something of a choirboy growing up. However, this choirboy was caught throwing spitballs down on the congregants, apparently incurring his father's wrath. I think Bob never lost that free spirit that enables him to connect with students. Role models like him are extraordinarily rare.

I hope the dean can convince him to unretire one more time.

*Gary V. Gordon, M.D. '73
Philadelphia, Penn.*



The first use of penicillin

To the Editor:

Your story on John F. Fulton ["Fulton, penicillin and chance," Fall 1999/Winter 2000] brought back memories. Perhaps you will permit me to add a few facts.

Dr. Fulton was Sterling Professor of Physiology at the time and not a clinician. The clinician who engineered the obtaining of some penicillin was Dr. Francis G. Blake, Sterling Professor of Medicine as well as the medical school's dean.

I recall many a night, as a senior intern on the isolation ward, walking from Fitkin (Dr. Blake's office) to Brady, where a filter was available courtesy of Dr. Morris Tager of Bacteriology, and back to isolation with the "precious product." It was necessary to filter the solution made from the yellow powder received from Merck in Rahway, N.J., to be certain there were no residual bacteria. This was then given to the patient, 5,000 units intravenously every four hours. Today we think nothing of giving a million or more units several times daily.

One of my clear memories is that of Dr. Wilder Tleson on rounds that Monday morning looking at the very graph of Mrs. Miller's chart you published and mumbling just loud enough for those of us close enough to hear, "Black magic!"

Your comment from Herb Tabor, M.D., was pertinent. You might have added that in addition to his distinguished career as a research biochemist, he has been senior editor of the *Journal of Biological Chemistry* for many years.

*Charles M. Grossman,
M.D., HS '44
Portland, Ore.*

More facts on Fulton

To the Editor:

I recently received the Fall 1999/Winter 2000 issue of Yale Medicine. On page 12, there is a picture of Drs. Fleming and Blake. I am not sure, but I think Dr. Blake is on the left and Fleming is on the right. The article mentions that Dr. Fulton was in the hospital at the same time Mrs. Miller was being treated for postpartum infection. It does not mention what Dr. Fulton was being treated for. We were told years ago that he had developed coccidioidomycosis following a visit to California and that the penicillin was originally intended for him, but he got well without it and it was then used for Mrs. Miller.

Finally I must make a comment about which I imagine you can do nothing. Having had bilateral cataract surgery recently and several changes of eyeglasses, I find that I still cannot see clearly. The print in the magazine is so small I must use a bright light and a magnifying glass to read it. Even this is only of partial assistance. I wonder if other older alumni have this problem and if it might be possible to use larger type?

*Paul R. Bruch, M.D. '51
Southbury, Conn.*

AP WIDE WORLD PHOTOS



Thanks to Dr. Bruch and others who wrote to correct the identification in the photograph. Dr. Blake is indeed pictured on the left. As for the size of Yale Medicine's body type, we are continuing to experiment with improvements to legibility. In addition, readers with access to the Internet may read the articles online (and control the type size via their Web browser) at info.med.yale.edu/lymm.

Easing children through surgery

To the Editor:

This letter is written in response to your article about the work of Zeev Kain. ["Easing children's minds about surgery," Fall 1999|Winter 2000.] I trained at Yale in the late 1950s, when there were no pediatric surgeons on the staff. After completing my training, including a year at Pittsburgh Children's Hospital, I returned to practice with Dick Selzer.

I was the first surgeon trained as a pediatric surgeon and had quite a time convincing the hospital and Blue Cross that outpatient surgery was a good thing for children and deserved coverage. Drs. Pickett, Toloukian and Seashore followed and established an excellent pediatric surgery section.

Besides the use of sedation, as the article mentioned, there are many other ways of reducing stress. Playing children's music in the operating room makes a big difference, too. It relaxes the children and the staff. However, I was deemed an explosion hazard the first time I showed up with my tape recorder, in the 1970s, when cyclopropane and ether were still in vogue.

I also have found that children are excellent subjects for hypnosis and that simple stories and suggestions will often change their attitudes toward surgery. A statement such as

"You'll be going out" can be scary if it is understood to mean "out of control." On the other hand, "You will go to sleep in the OR" induced sleep in several of my young patients almost instantly as they were wheeled to surgery. I often spoke to children and adults while under anesthesia because they hear and respond to the suggestions and information given them. I was considered crazy until the beneficial effects were seen. Then I got to present anesthesia grand rounds. As a matter of fact, my greatest compliment came from Dr. Jake Goldstein, who declared I was equal to 10 cc's of Pentothal.

Hopefully the surgeons are less of a problem today than in the past. If not, there are drugs available that could be helpful. Perhaps preoperative sedation for surgeons should be the next study undertaken.

*Bernie Siegel, M.D., HS '61
Woodbridge, Conn.*

P.S. I am always available for another grand rounds.

FRANK POOLE



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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 yym@yale.edu, and include a daytime telephone number. Submissions may be edited for length, style and content.

\$500 million for medicine

Corporation approves construction of Congress Avenue Building and a 10-year renovation plan.

After two years of incremental approvals, the Yale Corporation voted at its February meeting to construct a major new research and teaching facility on Congress Avenue as part of a plan to invest at least \$500 million in medical school facilities over the next 10 years.

Excavation of the site—a full block bounded by Congress and Howard avenues and Cedar and Gilbert streets—began in early March following demolition of the eight-story brick building at 350 Congress Ave. and several adjacent structures. University officials have signed a \$176 million contract for construction of the new Congress Avenue Building (CAB), with occupancy expected in March 2003. It is anticipated that the project will be supported in part by philanthropy.

“This is the largest single investment in a facility in Yale’s history,” President Richard C. Levin said of the new building when the decision was announced Feb. 24 before a large crowd of faculty and staff in the Medical Historical Library. “This is only the beginning of an important period of investment in the School of Medicine. By the end of the decade, we will have invested half a billion dollars in facilities here and have a scientific research capability that is second to none.”

The decision came a month after the announcement that the University would invest another \$500 million to construct and improve science and engineering facilities on the central campus, bringing the new investment in science during the next decade to \$1 billion. According to Levin, “For Yale to remain

Demolition of 350 Congress Avenue, January 26, 2000 >



JOHN CURTIS

Projected opening of new Congress Avenue Building, March 2003 >



DIGITAL IMAGE BY VISARC

among the very best universities, to be the best university in the world, we must be among the best in science. That is an imperative for the 21st century.”

The Congress Avenue Building—actually two wings joined by an atrium and central courtyard—will contain six floors of laboratories for disease-oriented research, core facilities for genomics and magnetic resonance imaging, a 140-seat auditorium, and state-of-the-art teaching space for anatomy and histology. In the final blueprints, the building measures 450,000 gross square feet and includes 136,600 net square feet of wet-bench laboratory, lab-support and research-office space.

Overall, the facilities plan will increase lab space at the medical school by 25 percent.

The announcement of the new building generated excitement across the medical school campus, which first looked to the Congress Avenue site for relief from its space shortage more than a decade ago. Dean David A. Kessler, M.D., drew a loud round of applause when he announced the March 2003 move-in date.

“There is no doubt,” he told the crowd, “that this investment will affect the future of the medical school and quicken the pace at which we can bring discoveries in the laboratories to the benefit of our patients. It will enhance our research space, our educational programs and the opportunities we can afford students, and it will help us sustain a brilliant and creative faculty as they literally transform the face of medicine.”

The decade-long facilities plan includes provisions to renovate existing laboratories throughout the medical school and to look carefully at the future use of space that will be made available when the future occupants of CAB move to the new building. Kessler said that the departments will have an opportunity to put forward requests and participate in the planning based on the school’s academic needs and priorities.

Smoke signals

Research unit to investigate why some tobacco users simply can’t quit.

For many, nicotine gum or the patch has tipped the balance in the struggle to quit smoking. Others try hypnosis or break the habit cold turkey. But for a significant subgroup of smokers who would like to stop, nothing seems to work. Yale researchers recently received a \$10 million grant to find out why.

The grant, from the National Institute on Drug Abuse, the National Cancer Institute and the Robert Wood Johnson Foundation, is part of a five-year, \$84 million nationwide plan to create tobacco research centers around the country in an effort to reduce tobacco use. Six other institutions have been awarded grants.

The new Transdisciplinary Tobacco Use Research Center at Yale, led by Stephanie O’Malley, Ph.D., professor of psychiatry, will undertake five research projects. “The goal of our center is to improve tobacco addiction treatment by studying why current treatments fail and developing new



behavioral and drug treatments that address these factors,” said O’Malley. The Yale studies will focus on three groups who are giving up smoking at a slower rate than the nation as a whole: female smokers, smokers with depression and smokers who drink heavily.

Robert B. Innis, M.D., Ph.D., professor of psychiatry and pharmacology, will use PET and SPECT imaging to improve understanding of brain systems altered by smoking. Suchitra Krishnan-Sarin, Ph.D., assistant professor of psychiatry, will study behavioral, biochemical and endocrine responses that follow smoking cessation. Peter Salovey, Ph.D., professor of psychology and of epidemiology and public health and in the Cancer Center, will compare the effectiveness of anti-smoking messages that emphasize the benefits of quitting and those that emphasize the risks of not quitting. Marina R. Picciotto, Ph.D., assistant professor of psychiatry and pharmacology, will study the biological bases of depression, heavy drinking and female gender in resistance to smoking cessation.

O’Malley will expand on previous studies that suggest that the drug naltrexone, used for alcohol dependence, may also help smokers quit when combined with a nicotine patch. “It is critically important that more effective smoking cessation treatments be developed,” O’Malley said, “because most smokers try to quit only once every three to four years.”

et cetera

THE INSTITUTE OF MEDICINE has honored two from Yale with senior membership. Pasko Rakic, M.D., Sc.D., the Dorys McConnell Duberg Professor of Neuroscience and chair of the Section of Neurobiology, and Lewis P. Rowland, M.D. ’48, HS ’50, professor of neurology at Columbia University in New York, were elected to the senior ranks in October. Among the 55 new members of the institute were four Yale alumni, including Yale College graduates David Ginsburg, M.D., Richard Hodes, M.D., and Jeffrey P. Koplan, M.D., M.P.H.; and Nancy Hopkins, Ph.D., a biologist who did her graduate work at Yale.

FAREWELL TO YPI
After almost 70 years, the Yale Psychiatric Institute is closing its doors, a victim of the new economics of health care. YPI’s functions will transfer from the School of Medicine to Yale-New Haven Hospital as soon as the change is approved by the state’s

Medical school gears up for Yale's 300th

With its own bicentennial only a decade away, the medical school has its sights set on a more immediate cause for celebration and reflection: the 300th anniversary of the founding of Yale College in 1701. The first of three University-wide Tercentennial weekend celebrations is planned for Oct. 21 of this year along the theme of "New Haven and Yale," with a number of open houses in laboratories, museums, classrooms and theaters across the University.

The second anchor celebration will take place April 20-22, 2001, around the theme "300 Years of Creativity and Discovery" at Yale. The culminating events of the Tercentennial will occur Oct. 5-7, 2001, the weekend closest to the anniversary of the signing of Yale's charter.

The medical campus will join in the opening of the Tercentennial in October with events exploring the themes of "Community Outreach," "Teaching What We Do" and "Engaging the Public." In a series of exhibits, demonstrations, hands-on activities and lectures, the public will have a chance to learn how to conduct a physical exam, explore

the body using virtual anatomy software and peer at molecules through an electron microscope. A photographic exhibit will chronicle the activities of students and faculty who volunteer their time and skills in service of New Haven. Under the category of "Teaching What We Do," the public is invited to a series of activities which include a visit to the Magnetic Resonance Center and an anatomy class for young children. The Historical Library is planning a lecture series and a display of historic prints by early medical practitioners Fry and Vesalius.

In November playwright and performer Anna Deveare Smith will create a theater piece based on interviews with patients, physicians, caregivers and others at Yale-New Haven Hospital and the School of Medicine. She will perform the piece at grand rounds during the week of Nov. 13.

Harris Building opens its doors

The Yale Child Study Center, which has a long and distinguished history of research and clinical work with children and families from around the world, dedicated the new Neison and Irving Harris Building in October.

Founded in 1911 by Arnold Gesell, the center has expanded its mission over the years to include a wide array of programs ranging from basic studies of developmental neurobiology and genetics to therapeutic programs in schools and the community. The new 21,000-square-foot Harris Building will house many of the center's research and community programs including the Child Development and Community Policing Program, the Comer School Development Program, and the range of research and clinical programs for very young children.

The building was the gift of Neison and Irving Harris, Yale College graduates who have had a long-standing interest in the welfare of children and have been friends and supporters of the Child Study Center for many years. The Harris family and many others have joined together in their concern for children and families and their trust in the work of the Child Study Center. According to Director Donald J. Cohen, M.D. '66, the building will help raise the profile of children's issues. "The idea is that medical students and undergraduates will see the Yale Child Study Center and recognize that the child and family are essential to their education, regardless of what field they go into."

Guests at the opening on Oct. 14 included Irving and Joan Harris, New Haven Mayor John DeStefano, Dean David A. Kessler, and Yale President Richard C. Levin.

Guests at the opening of the new Harris Building filled its auditorium to capacity.



MICHAEL MARSLAND

YCC director will guide revision of National Cancer Act



DeVita

In the 29 years since the Nixon administration and Congress declared war on cancer with the passage of the National Cancer Act, physicians and scientists have discerned cancer's origins, found ways to treat it and made previously lethal forms of it manageable. Now a Senate advisory committee is looking at ways to update the act to incorporate this new knowledge. Leading the committee as co-chair is Vincent T. DeVita Jr., M.D., director of the Yale Cancer Center and one of the nation's leading cancer experts. "Our knowledge of cancer, cancer research and cancer control have changed substantially since the original National Cancer Act was enacted," says DeVita, who believes cancer may someday be

managed as a chronic disease. He served as director of the National Cancer Institute for nine years under presidents Carter and Reagan. "I look forward to uniting the cancer community to formulate a new blueprint for the war on cancer."

The 20-member committee, which will meet monthly throughout the year, includes physicians, scientists, business leaders, insurance executives and people with cancer. Sen. Dianne Feinstein, a Democrat from California, asked DeVita to serve on the committee. The advisory committee will work with the National Dialogue on Cancer (NDC), of which DeVita is also a member. The NDC is led by former President George Bush and brings together people in public, private and non-profit organizations dedicated to eradicating cancer.

Work of early cancer virologist celebrated at symposium

The human papilloma virus (HPV) infects thousands of men and women each year. Symptoms seldom appear, but for women it remains a potential threat later in life. Under certain conditions, its presence can suggest a higher risk of cervical cancer.

Because it serves as an example of a link between viruses and cancer, HPV was chosen as the topic of a symposium in December to honor Francesc Duran i Reynals, M.D., one of the first researchers to explore cancer's viral origins. Duran i Reynals was a member of the Yale faculty from 1938 until his death from cancer in 1958. The Francesc Duran i Reynals Symposium, sponsored by the Yale Cancer Center, commemorated the centenary of the physician's birth in Barcelona in 1899.

While still a medical student in Spain, Duran i Reynals joined the microbiology laboratory of renowned researcher Ramon Turro. In 1925, Duran i Reynals became the first Spanish scientist to culture bacterial viruses. He became convinced that viruses could cause cancer and secured a fellowship at Rockefeller University to pursue his research. His work there and in New Haven shaped the study of tumor biology.

Speakers at the symposium included José Costa, M.D., professor and vice chair of pathology; Josep M. Borrás, M.D., director of the Catalan Institute of Oncology; Xavier Bosch, M.D., chief of epidemiology service at the Catalan Institute of Oncology; Daniel DiMaio, M.D., professor and vice chair of genetics; and Carlos Cordon-Cardo, M.D., director of the Division of Molecular Pathology at Memorial Sloan-Kettering Cancer Center. Dean David A. Kessler offered closing remarks for the symposium, which was attended by members and friends of the Duran i Reynals family.



Maria Luisa Duran i Reynals attended the symposium honoring her late husband. The locket, engraved with the date of the event, was a gift from the Cancer Center.

Office of Health Care Access. William H. Sledge, M.D., assistant chief of psychiatry at the hospital, will be medical director of the new facility, which will be known as the Yale-New Haven Psychiatric Hospital and will occupy the same Frank Gehry-designed building on the corner of Cedar Street and Congress Avenue. Sledge said three factors led to the decision to close YPI. Yale-New Haven Hospital has more access to patients through its medical services and can participate in federal programs such as Medicare and Medicaid more fully than a free-standing psychiatric hospital. "The other part of it is that it is very inefficient to have two psychiatric services operating side by side and duplicating a lot of the overhead and other support services," Sledge said. And, he added, a free-standing psychiatric institute lacks the negotiating clout of a hospital that's part of a larger health care system.

A SPINOFF FROM THE LAB

The Office of Cooperative Research has struck a deal with a Science Park biotech firm to distribute new reagents created during the course of University research. Recombinant Technologies, founded by associate research scientist Pazhani Sundaram, Ph.D., of the School of Public Health, will work with the University to identify commercially viable reagents and negotiate their distribution to researchers.



Malaria, transmitted by mosquitoes but rarely seen in the developed world, kills 1.5 million people each year in southern Asia, Africa and Latin America. The two cases reported in New Haven in late 1999 were contracted abroad.

Malaria makes a comeback, even in the U.S.

When two cases of malaria surfaced in New Haven late last year, they were of interest to clinicians not because of any epidemiological threat, but for the treatment problems they posed. Both cases were imported, rather than transmitted within North America. Both patients had contracted malaria during visits to West Africa to visit family. One was 24 weeks pregnant and one was found to be HIV-positive.

The clinicians treating the HIV-positive patient, according to Frank J. Bia, M.D., M.P.H., professor of medicine and laboratory medicine, speaking at grand rounds in January, were concerned about the interactions between HIV infection and malaria. In the case of the pregnant patient, noted Marissa Wilck, M.D., Winchester Fellow in Clinical Microbiology, clinicians were interested in the interaction of hemoglobinopathy and malaria. Ultrasound revealed the woman's fetus to be healthy.

A distant memory in the developed world, malaria is thriving in 91 countries (See cover story, page 16). In southern Asia, Africa and Latin America, malaria affects about 300 million people annually and kills as many as 1.5 million each year, mostly children. Malaria has defeated eradication efforts, which were abandoned 30 years ago in favor of control strategies. It has become resistant to synthetic cures such as chloroquine and, with increased ease of travel, threatens to reach places where it was thought to be done away with. It is not unusual to see imported cases at Yale-New Haven Hospital, Wilck said. New York City, with its large population of immigrants, Bia said, has reported cases of transmitted, as well as imported, malaria.

Western medicine first found a remedy for malaria in the 17th century, when a Jesuit missionary in Peru was cured with the bark of the cinchona tree. It was thereafter known as Jesuit's bark or Peruvian bark. Its active ingredient was quinine.

The pathogen's portal into the body remained a mystery until 1898, when Ronald Ross, a British physician with the India Medical Service, identified the female *Anopheles* mosquito as a vector. Malaria is believed to be 30 million years old, and humans are not its only vertebrate target. Other primates, even birds, have their own forms of malaria infection.

Ultrasound provides an alternative to amnio

Yale scientists have devised a test for fetal anemia that eliminates the risks of invasive procedures such as amniocentesis or cordocentesis. The test uses Doppler ultrasound to measure fetal blood velocity in the cerebral circulation. Anemic fetuses have a higher blood flow velocity in arteries and veins. "Invasive procedures place the fetus in unnecessary danger," said Giancarlo Mari, M.D., associate professor of

obstetrics and gynecology and lead author of the study. "In more than 70 percent of cases, the fetuses tested were either non-anemic or mildly anemic, and an invasive procedure could have been either avoided or delayed." The study was published in the Jan. 6 issue of *The New England Journal of Medicine*.

Is it ever right to practice on the dying?

Early in 1998 a student approached Lauris C. Kaldjian, M.D., HS '91, with a question about something disturbing seen on the wards. The student, said Kaldjian, wondered if it was ethical to use a dying patient to practice inserting a femoral-vein catheter, even though the procedure offered no therapeutic value.



Kaldjian

"There was enough of a concern to do a proper study of the question," said Kaldjian, a clinical instructor in medicine who co-directs a program on ethics for hospital residents and

is pursuing a doctorate in ethics at Yale's Department of Religious Studies. In the fall of 1998 Kaldjian surveyed 234 residents at three training programs encompassing five hospitals in Connecticut. "I was surprised that as many as a third of the respondents thought it was appropriate to use one patient for the sake of other patients," he said. "The important thing to remember is that the people who believe this is OK are doing this for noble reasons. The question is, 'Can one have good motivations and still be doing something that is inappropriate?'"

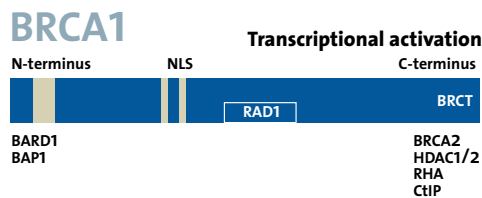
In a paper published in the Dec. 30 issue of *The New England Journal of Medicine*, Kaldjian reported that 34 percent of respondents believe it is sometimes appropriate to insert femoral-vein catheters for practice during cardiopulmonary resuscitation, 26 percent had observed such insertions and 16 percent had attempted the procedure themselves. "We don't see any

reason to doubt that results would be different elsewhere," Kaldjian said.

The dilemma, he says, is to reconcile the needs of the patient with the larger need of society to have well-trained doctors. "I would argue that, as a clinician, my first responsibility is to the patient who is immediately in front of me. We cannot use one patient to serve other patients," he said, noting that there are alternatives to this way of training. "You learn to do this procedure on people who have to have it done."

Breast-cancer genes factor into treatment

Young women with breast cancer who carry either of two mutated genes may be at higher risk for a new cancer years after initial treatment, according to a study by Yale researchers. "Our findings reveal that if these women elect breast-conserving therapy—radiation and lumpectomy—there is possibly a greater risk of developing a second tumor in the conservatively treated breast," said Bruce G. Haffty, M.D., associate professor of therapeutic radiology. The genes, *BRCA1* and *BRCA2*, are passed from mother to daughter, and previous studies have shown that women who carry them have higher-than-normal rates of breast cancer. "Young age is often associated with BRCA abnormalities. If these women are predisposed to cancer, then trying to suppress it in some fashion would make sense," Haffty said. The findings were published in the October issue of the *Journal of Clinical Oncology*. Haffty has begun a larger study, looking at up to 150 women aged 42 or younger.



Women who carry the *BRCA1* gene, shown above in a schematic representation, have higher-than-normal rates of breast cancer.

DR. DOE DECISION IS REVERSED

Connecticut's Supreme Court has thrown out a \$12.2 million award to a former hospital intern who was infected with HIV after an accidental needle prick. In dismissing the damage award, the court also ordered a new trial in the case. The intern, known in court papers as Dr. Doe, sued the University and Yale-New Haven Hospital and claimed that the incident was the result of inadequate training and supervision. She pricked herself in 1988 while inserting a line into a patient with AIDS.

The state Supreme Court ruled that the original trial judge erred in ruling out the University's claim of immunity under workers' compensation laws. The judge also failed to instruct the jury that its verdict must be based on expert testimony, the court ruled.

BRING IN THE MARINE SPONGES

A Yale chemistry professor is looking at natural products from a Western Pacific marine sponge as a potential source of chemotherapeutic agents. David J. Austin, Ph.D., has received a three-year, \$150,000 grant from the Johnson & Johnson Focused Giving Program, which funds health care and medical research by academic scientists. Austin plans to use the grant to synthesize palau'mine, a sponge found off the Palau Islands, and evaluate its biological effects.

ILLUSTRATION: BRUCE HAFFTY AND PETER JOHNSON



Aspirin in combination with the blood-thinning agent Coumadin has been widely regarded as an effective measure to prevent clotting in the coronary arteries after a heart attack. Yale investigators examined data from 5,000 cases over a six-year period and concluded that aspirin alone works just as well as the combination therapy.

Aspirin, on its own, shown to reduce heart-attack risk

An aspirin a day is as effective alone as with a powerful drug at preventing blood clotting in coronary vessels after a heart attack, Yale researchers have found. The six-year study of more than 5,000 subjects found no difference between heart-attack sufferers who used aspirin alone and those who used it in combination with the anti-clotting drug Coumadin. "There was no difference between the two groups in terms of total mortality, cardiovascular mortality, non-fatal myocardial infarction and non-fatal stroke," said Michael Ezekowitz, M.D., professor of medicine and cardiology. Aspirin is cheaper than Coumadin and does not require monitoring. The study was presented at the American Heart Association meeting in November.

Antibody test is a reliable screen for ehrlichiosis

A collaboration between scientists at Yale and the State of Connecticut has yielded a simpler and more reliable blood test to diagnose ehrlichiosis. The disease, carried by the same deer tick that spreads Lyme disease, causes flu-like symptoms such as headache, fever and muscle cramps. It is not known if it can cause any long-term health problems. Jacob IJdo, M.D., and Erol Fikrig, M.D., collaborated with Louis Magnarelli, Ph.D., vice director of the Connecticut Agricultural Experiment Station in New Haven, in developing a test that seeks out antibodies specific to ehrlichiosis. Their findings were published in the November issue of the *Journal of Clinical Microbiology*.

Much heralded medication for autism is ineffective

A drug thought to work marvels on autistic children has no more effect than a placebo, according to a Yale psychiatrist. In an editorial commenting on a study published Dec. 9 in

The New England Journal of Medicine which found secretin no more effective than a placebo, Fred Volkmar, M.D., professor of child psychiatry, noted the considerable interest in the use of secretin, a hormone used to treat gastrointestinal problems, generated by the media. "There is no evidence that it works," Volkmar said. "There is no reason to think that it would have worked in the first place." Autism, which affects one child in 2,000, is a brain disorder that results in impaired or delayed social and communication skills. There is no known cure, but early educational and behavioral intervention can significantly facilitate outcome.

A new therapy for prostate cancer

A new radioactive isotope, palladium-103, used for radiation implant therapy for early prostate cancer has proven as effective as an older and more common therapy, but with fewer long-term side effects, a Yale study has found. "The overall cure rates using palladium-103 or iodine-125 appear very similar," said Richard Peschel, M.D., professor of therapeutic radiology. "However, the newer palladium-103 treatment was better than iodine-125 at preventing both moderate and severe long-term complications." Peschel tracked 150 patients over seven years for his study, which was published in the Oct. 29 issue of *Radiation Oncology Investigations*. Peschel attributed the difference in side effects to the higher dose rate for palladium-103. Palladium doses are given over two months as opposed to six months for iodine.



RAMOS-HORTA



HASELTINE



VERMA



PRUSINER

JOHN CURTIS (4)

Human rights in East Timor

Freedom for East Timor has come at a heavy price. When an overwhelming majority of East Timorese cast ballots for independence in August, retribution from their Indonesian conquerors was swift. A wave of violence left between 70 and 80 percent of the country's buildings in ashes and up to 10 percent of its 850,000 inhabitants missing or displaced. In November, resistance leader José Ramos-Horta (1) stopped at Yale to speak at a conference on East Timor sponsored by the Yale-Griffin Center for Health and Human Rights and the Health and Human Rights Committee of the Department of Epidemiology and Public Health. He was once asked, he said, if the struggle for freedom was worth a single human life. "If the people of East Timor manage to build a society that is free of abuse, a country based on the rule of law, a country of genuine equality," said Ramos-Horta, co-winner of the 1996 Nobel Peace Prize, "if we are able to build a country where everyone has basic necessities, where everyone has access to education, health care and good nutrition, then maybe I will say it was worth it."

Is sex important?

Getting women's health issues on the national radar, Florence Haseltine, M.D., (2) said during a visit to Yale in October, first meant taking sex out of the equation. "Ten years ago, two headlines related to women," she quipped, "PMS leads to murder and the pill causes cancer." Haseltine, a gynecologist and director of the Center for Population Research at the National Institute of Child Health and Human Development, said health institutions dominated by men and the largely male U.S. Congress were leery of anything related to sex. The key to bringing attention to women's health issues resided in a simple statistic. Most medications for women are taken by women over 50. Researchers decided to eliminate from study women under 50, Haseltine said. "That got rid of sex," she told mem-

bers of the Yale-New Haven Hospital Auxiliary, which sponsored her talk, "Is Sex Important?" "You don't have kids, you don't have abortions and you don't have sex. That's wrong, but it's the reality in Washington."

HIV as a cure rather than a threat

When Inder Verma, Ph.D., (3) proposed HIV as a vector for gene therapy two years ago, the response was swift. "This guy must be nuts," Verma said, describing the initial reaction. "Why would he put HIV vectors into people?" But Verma, a researcher at the Salk Institute for Biological Studies, saw that HIV could overcome problems inherent in other viral vectors because it can both elude the immune system and integrate into non-dividing cells such as those in the liver and brain. He has had some success with the HIV vector in animal models. In his talk in November sponsored by the Department of Molecular Biophysics and Biochemistry, he said he has eliminated the proteins in HIV that make it pathogenic. "We believe it is as safe as we can make it in terms of its ability to cause disease."

Prions, mad cows and the Nobel Prize

For Stanley B. Prusiner, M.D., (4) vindication came in 1997 when he won the Nobel Prize in Physiology or Medicine for his discovery of the potentially infectious proteins he called prions. During the 20 years leading up to the honor, Prusiner was seen as a heretic for his view that "rogue" proteins could cause disease. "How is it that a protein can be infectious?" asked Prusiner, professor of neurology, virology and biochemistry at the University of California, San Francisco, during a visit to the medical school in November. The ubiquitous and normally harmless prions, Prusiner found, can take on an abnormal conformation and set off a chain reaction of malformed cells that trigger diseases of the brain, such as scrapie in sheep, mad cow disease and Creutzfeldt-Jakob disease. Prusiner is now looking for compounds that will thwart prions' pathogenesis.

In yeast studies, a mutated DNA reveals location, function of genes

Yale researchers have discerned the functions of a third of the genes in the yeast genome, using a novel method of DNA insertion that can be applied to other organisms. The new tool will allow researchers not only to identify genes, said principal investigator Michael Snyder, Ph.D., but figure out what they do. “That is going to be the next big challenge,” he said. Snyder and his interdisciplinary team followed, using chemical markers, a mutated, bacterially derived strain of DNA as it interacted with yeast genes and proteins. They observed at what point in the yeast’s life cycle genes were expressed, where in the cell proteins were located and what disruptions the mutated DNA caused. Their results were published in the Nov. 25 issue of the journal *Nature*.

Mitochondrial voltage and neural connections

Mitochondria are not only the energy packs of each living cell, but also judge and jury, deciding whether cells live or die. Given that power, aberrant mitochondria have long been suspects in degenerative diseases such as Parkinson’s, in which cells die and crucial neural connections

are lost. The strength of those connections depends on electrical activity in the mitochondria—the higher the activity, the stronger the links.

Now Yale researchers have become the first to record electrical activity in the mitochondria of living cells.

By inserting microscopically thin glass pipettes into squid cells, which are large and easy to manipulate, researcher Elizabeth A. Jonas, M.D., was able to stimu-

late the nerve cells with electricity for one or two seconds. Mitochondria in those cells seemed to “remember” the stimulation for 30 seconds or more. “Mitochondria have had less attention paid to them than they deserve,” said principal investigator Leonard Kaczmarek, Ph.D., professor of pharmacology. “We think they are very important in determining the strength of the connections.” The study was published in the journal *Science* on Nov. 12.

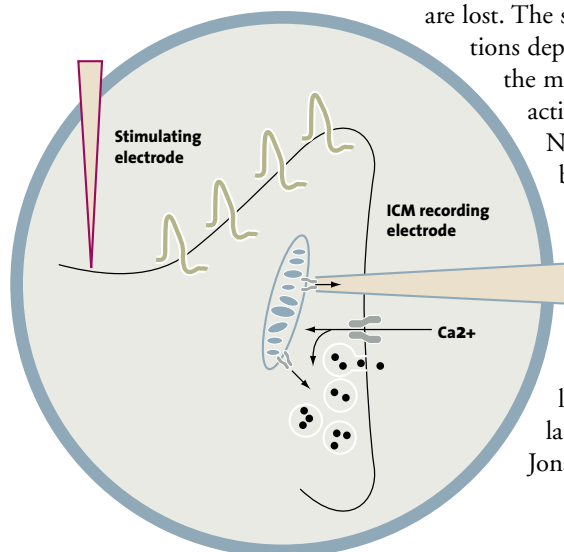
A role for serotonin in long-term memory

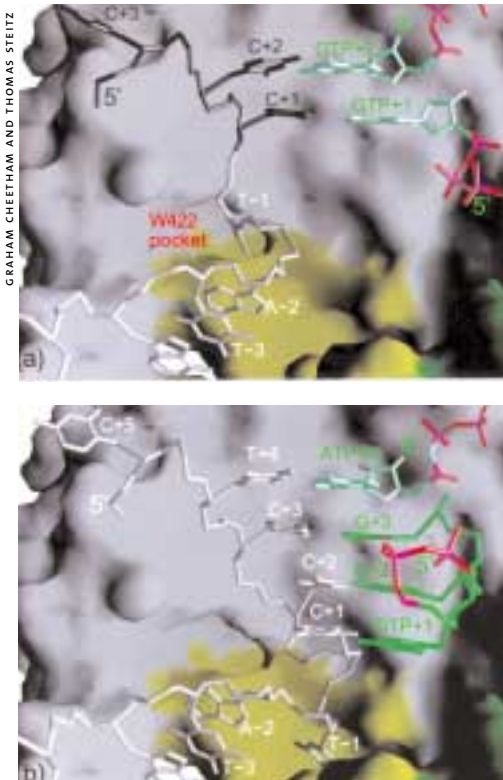
Yale scientists have discovered a new mechanism for strengthening synapses that store long-term memories. Applying the neurotransmitter serotonin to pre-synaptic and post-synaptic cells in the sea slug *Aplysia* strengthened the synapse if both cells received the serotonin within 15 minutes of each other. Researchers had previously determined that serotonin, which is linked to aggression and depression in mammals, also would strengthen synapses when applied in sufficient quantities to pre-synaptic cells. In the more recent experiments, the researchers applied to both pre-synaptic and post-synaptic cells amounts of serotonin too small to induce long-term memory when applied to one cell alone. “It’s a new way of signal processing within a cell that is different than what we had thought of before,” said neurobiologist Carolyn Sherff, Ph.D., a postdoctoral associate and co-author of the study with Thomas Carew, Ph.D., professor of psychology and molecular, cellular and developmental biology. Their study was published Sept. 17 in the journal *Science*.

At last, a close-up view of the transcription process

In a discovery that offers insights into fundamental cellular processes, Yale researchers have observed for the first time the transcription of genetic information from a DNA template to viral RNA. “In general,” says Thomas A. Steitz, Ph.D., professor of molecular biophysics and biochemistry, “the initiation of transcription of DNA into RNA is one of the

Scientists in the Department of Pharmacology are the first to have recorded electrical activity in mitochondria of living cells. **BELOW:** the pathway used to stimulate and record electrical activity in mitochondria.





Crunch time: X-ray crystallography reveals new details of the transcription process. These images show the movement of an RNA template as it accumulates genetic information.

most heavily regulated steps in cells. It is what makes one cell different from another.” Steitz called the initiation events, observed through X-ray crystallography, “scrunching.” The DNA, he said, coils like a rope inside the enzyme polymerase, accumulating in the enzyme’s active site as the first short RNA transcript is being synthesized. The findings were published in the journal *Science* on Dec. 17.

Shedding light on *Salmonella*’s Trojan Horse

To invade and occupy a cell, *Salmonella* first deploys a Trojan horse, a protein called SopE that instructs the cell to internalize the bacterium. If left unchecked, however, this protein will destroy the host and deny the *Salmonella* a safe haven from which to replicate, penetrate

deeper tissues and ward off attacks from the immune system. Researchers in Yale’s Section of Microbial Pathogenesis, who previously discovered a second *Salmonella* protein, SptP, have now discerned its function. SptP protects *Salmonella*’s new home by reversing the destructive process started by SopE. “These findings bring us closer to understanding the complex mechanisms by which these bacteria cause disease and may lead to development of new therapeutic and prevention strategies,” said Jorge E. Galan, Ph.D., who heads the section. The findings were published Sept. 16 in the journal *Nature*.

New role found for B Cells in gastrointestinal disease

A team of Yale researchers has traced a path of cellular development that may lead to gastrointestinal and other ailments, including Creutzfeldt-Jakob disease, which is related to mad cow disease. The trail starts with the B cell, once thought capable only of producing serum antibodies and activating T lymphocytes. Now researchers have found that B cells are necessary for development of the M cell, an intermediary between the body and organisms in the gut. Only some of the M cell’s functions have been discerned. “M cells play a role in sensitizing the immune system to gastrointestinal flora,” said Mark Shlomchik, M.D., Ph.D., associate professor of laboratory medicine and immunobiology, “but they are also a portal of entry since many pathogens seem to enter the body through M cells.” The work, done in collaboration with a team at Jackson Labs, was published in the Dec. 2 issue of the journal *Science*.

DR. MEL’S DOCTORS
Connecticut’s best-known meteorologist is donating the proceeds from his best-selling book, *The Complete Idiot’s Guide to the Weather*, to the Yale Cancer Center. Dr. Mel Goldstein was diagnosed three years ago with a rare cancer of the bone marrow and credits his care at the cancer center with keeping him alive since then. His treatment has included a combination therapy using thalidomide, the compound that caused birth defects when used by pregnant women in the early 1960s, but which recently has shown promise as a cancer drug. Proceeds from the book will benefit the Dr. Mel Goldstein Multiple Myeloma Research Fund.

INFORMATICS INITIATIVE
The Center for Medical Informatics plans to use a \$1.5 million grant it was awarded last year to develop a computer system to analyze and compare tumor cells. The grant from the National Library of Medicine will allow researchers to test the Next Generation Internet using PathMaster, a software being developed at Yale to analyze cell images. Lymphoma and thyroid cells will be studied. As part of the project, the center will expand its database of malignant-cell images from 500 to 30,000 over the next three years, according to Director Perry L. Miller, M.D., Ph.D.

CAPSULE



PHOTOGRAPHS COURTESY CONNECTICUT HISTORICAL SOCIETY AND CONNECTICUT STATE LIBRARY/STATE ARCHIVES; LOUISE BURR

A tragedy's medical aftermath

Sorting through her late father's papers, the daughter of Albert S. Atwood, M.D. '45, found a letter written shortly after the Hartford circus fire of 1944, in which 168 people died. Atwood and five med school classmates dropped everything and drove to Hartford to tend to the hundreds of burn victims. When his letter surfaced, Atwood's classmates began exchanging reminiscences of the fire.

By John Curtis

July 6, 1944, a month after D-Day: More than 6,000 people sat under the Ringling Brothers Circus big top in Hartford, waiting for the Flying Wallendas to begin their trapeze act. Lions, tigers and leopards had just leapt into their cages. Almost no one noticed the tiny flame that crept up a side wall in a corner of the tent. A policeman described it as no bigger than a cigarette burn until it burst into flame.

The fire raced up the sides and along the top of the tent. Burning patches of canvas fell on the screaming spectators, who rushed in all directions looking for a way out. Within minutes, the tent was gone and hundreds of people lay piled on the ground, some dead, others dying, hundreds severely burned.

Word of the tragedy reached Louise H. Burr, M.D. '45, at Nick's Restaurant, a popular student eatery on Congress Avenue where dinner could be had for less than 50 cents. "Joe Stanton, a classmate, and I decided that with so many casualties there would no doubt be a great need for people trained to do blood counts, give plasma infusions, etc.," Burr wrote to her family a few days later.

"We hopped into a car, bringing our microscopes, blood-counting equipment and hematocrit tubes with us, and were off," wrote Albert S. Atwood, M.D. '45. The unsung hero of the adventure was Michael W. Lau, M.D. '45, who had a Ford



John Curtis is a staff writer for *Yale Medicine*.

convertible and, more important, coupons for rationed wartime gasoline.

The students went first to Hartford Hospital, where they were shocked to find 40 doctors and residents lounging on the grass outside. Only a few patients had arrived and there was nothing for them to do, the doctors and residents told the students. They continued to the now-defunct Hartford Municipal Hospital. “We arrived there to confront total chaos,” wrote James D. Gardam, M.D. ’45. “Relatives, cops, spectators, newspeople, untreated patients waiting for assistance.”

Two students were assigned to each of the three floors handling burn victims. Atwood went to the fifth floor with Stanton, where “it looked as if all bedlam had broken loose. Nurses and nurses’ aides were everywhere, as well as bewildered parents.” Hospital staff assigned the students to check vital signs and administer parenteral fluids where needed. “It sounded very easy but we were soon to find that it was anything but that,” Atwood wrote.

Emergency-room doctors had applied pressure dressings to the burns, which blocked access to veins for injections and blood-pressure readings. “On only a few could we get blood pressures because practically all arms and legs were in plaster casts,” Burr wrote. “They had received the following treatment: morphine, tetanus shots, vaseline gauze with plaster casts (for pressure), plasma and, later, sulfa-diazine.”

At 1 a.m. the medical students were reassigned to assist staff members on the floors. They made rounds with the patients while hospital staff prescribed sulfa drugs and fluids. At 3:30 most of the hospital staff left, leaving the wards in the hands of the six students. “It was really amazing,” wrote Atwood, “for we couldn’t imagine anyone leaving their hospital floors in complete charge of strangers who said that they were medical students.”

Not all hospital staff left. Nurses and aides stayed, as did a doctor in industrial medicine at Colt Firearms Company. A Navy corpsman home on furlough who was helping out said nothing he had seen on Guadalcanal affected him as much as the fire victims.

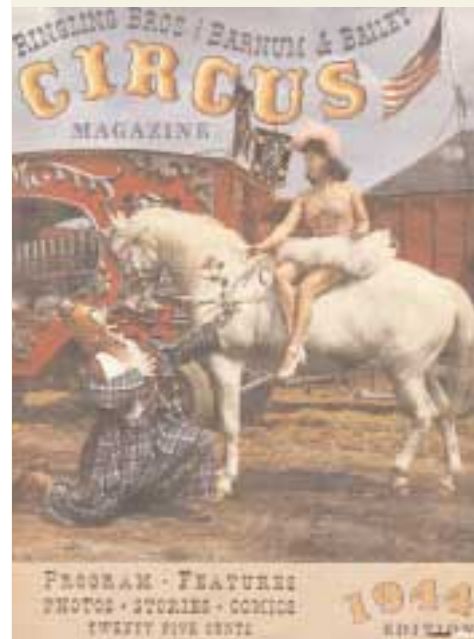
Fortunately for the medical students, shortly before the hospital staff retired, nine classmates arrived to help. “We did blood counts, hematocrits, gave plasma and sulfa-diazine infusions, ordered oxygen tents, morphine and sponges,” Burr wrote. “It seemed as if most of our time was spent trying to get needles into tiny foot veins. Several of the children died during the night and that, of course, was heartbreaking.”

Orangeade, coffee, sandwiches and donuts kept the students going. “About 4 a.m. I began to get my second wind,” Burr wrote. “By eight o’clock I was feeling fine except for blurry eyes and an occasional feeling that I wanted to cry on somebody’s shoulder.”

The students left at 11 a.m. and took a detour to the scene of the fire before returning to New Haven. The fire’s final tally was 168 dead, with hundreds more injured. For years the cause of the fire remained the subject of speculation—a carelessly tossed cigarette, an electrical short-circuit—until in 1950 a man admitted to setting the fire. He later recanted, however, saying his confession was coerced. At the time five circus managers were charged with manslaughter and sent to prison. Ringling devoted its profits for the next 10 years to paying off claims from victims’ families.

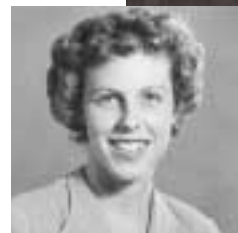
“It was a tremendous experience,” Burr said during an interview 55 years later. “It made me feel good that we did it and were able to help. It made me glad that I decided to go into medicine.”

Gardam said two distinct lessons came out of the experience. “Never give up venous access,” he said, “and have somebody in command.”



ABOVE: A program and ticket stub from the July 6 performance.

BELOW: Within hours, news of the disaster had reached New Haven and prompted six Yale medical students (including Louise Burr, inset) to hop in a car and try to help the injured and dying. A nurse in one of Hartford’s hospitals cared for a bandaged young patient, one of the less severely injured.



OPPOSITE PAGE: Within minutes of its eruption, the fire that engulfed the big top in Hartford on July 6, 1944, laid open the tent’s framework and sent those who could run scurrying for safety. A photograph taken during the first few minutes shows the enclosure filling with smoke.

BY BREAKING DOWN THE COMPLEX CYCLE THAT ALLOWS MOSQUITOES, TSETSE FLIES, TICKS AND OTHER ARTHROPODS TO TRANSMIT FATAL DISEASE, YALE SCIENTISTS ARE PROVIDING NEW AMMUNITION IN THE FIGHT AGAINST MALARIA AND OTHER VECTOR-BORNE ILLNESSES. **By Cathy Shufro**

To the vector go the spoils



AP/WIDE WORLD PHOTOS



Last July, something went very wrong in New York City's crow population. Signs of trouble appeared first in the Bronx, where birds were observed flying erratically, staggering on the ground and suffering convulsions. Before long, crow carcasses began to dot the landscape near the 265-acre Bronx Zoo, much to the alarm of its veterinarians. They had good reason to worry.

Around the same time that birds were dying in the Bronx, a disease with similar neurological symptoms was affecting humans in New York. The Centers for Disease Control and Prevention (CDC) identified it at first as St. Louis encephalitis, a viral infection carried by mosquitoes. The CDC suggested that the

deaths of birds, including flamingos, pheasants, cormorants and a bald eagle at the zoo, had been caused by mosquito-borne Eastern equine encephalitis, a disease that also affects horses and people. But Tracey McNamara, D.V.M., the zoo's chief of pathology, had her doubts. Although Eastern equine encephalitis does kill birds, the birds at the zoo that would have been most susceptible were all healthy. Australian emus, considered "sentinel birds" for the disease, showed no signs of illness.

By late September the CDC had arrived at a new diagnosis: Both the human and the avian deaths had been caused by West Nile virus, a mosquito-borne disease never before seen in the Western Hemisphere. By the end of sum-



GALE ZUCKER



mer, West Nile encephalitis would kill not only the zoo's birds and thousands of crows, but humans as well. Six New Yorkers and a Canadian tourist were dead, and 52 others had fallen ill.

The sudden appearance of West Nile in New York is yet another indication that the battle against infectious disease is far from over, says Durland Fish, Ph.D., an associate professor of epidemiology who has been a frequent commentator on the West Nile outbreak. A generation ago, as medicine marveled at the dramatic successes of antibiotics and the first effective vaccines, it seemed that communicable disease was on the way out. But in the last decade, the emergence of new maladies in

the industrialized world, along with new strains of bacteria resistant to antibiotics, has changed that picture.

Many of the emerging diseases are vector-borne, which is to say that they rely on a complex cycle of transmission enabled by intermediaries. These "vectors" include mosquitoes (which carry the West Nile virus and the protozoan responsible for malaria), sand flies, ticks and other arthropods. Vector-borne illnesses from Lyme disease to African sleeping sickness have been on the rise around the globe and resurgent in places where they had once been controlled.

"The wealthiest people in the world, living near New York City, and amongst the poorest

ABOVE: Irene Kasumba, left, and Leyla Akman hold cages for rearing tsetse flies in the newly constructed insectary at the School of Public Health. The \$700,000, state-of-the-art containment facility also holds the only colony of tsetse flies in North America.

OPPOSITE PAGE: A helicopter sprays for mosquitoes in New York City last September during the height of concern over West Nile virus



Boxes of dead crows piled up on the doorstep of state wildlife pathologist Ward Stone, above, as veterinarians from around the New York City region shipped them to his lab in Delmar, N.Y., for analysis last fall.

people in the world, living in rural communities in sub-Saharan Africa, all have to deal with vector-borne disease,” says Scott L. O’Neill, Ph.D., associate professor and head of the vector biology section at the School of Public Health. “It’s a universal problem.”

Vector-borne diseases are re-emerging, not only because insects have developed resistance to pesticides, and pathogens to medication, but also because war, human migration, poverty and complacency have undermined many of the disease-control strategies that were once effective. In addition, diseases are spreading to new places through international trade, travel and refugee resettlement. Patterns of disease may also be altering because of global warming, deforestation and even reforestation (as in New England, where the growth of new forest brings deer hosts for the tick responsible for Lyme disease into close contact with people).

The human cost of West Nile is dwarfed by the devastation caused by other vector-borne diseases, major killers. Malaria sickens 300 to 500 million people each year, according to the World Health Organization, and kills an estimated 2 million people annually—roughly the population of metropolitan Denver. Half of those who die are children. Other serious diseases, including yellow fever and dengue, are transmitted by mosquitoes. Tsetse flies spread fatal African sleeping sickness, and sand flies carry the protozoan responsible for two forms of leishmaniasis; the less deadly form, causing disfiguring skin infections, was contracted by some Gulf War veterans. A triatomid com-

monly called the “kissing bug” transmits the pathogen for Chagas’ disease, which can lead to encephalitis and heart disorders. Ticks carry not only the Lyme disease spirochete (which causes chronic neurological and joint problems in some patients), but also pathogens for two diseases newly discovered in the northeastern U.S., ehrlichiosis and babesiosis.

To counter these threats, vector biologists at Yale are developing novel strategies, drawing on fundamental new information about the genetic and molecular bases of these disease-transmission systems. It’s a strategy that looks at disease from many angles and incorporates entomology, molecular biology, field ecology, parasitology, population genetics and taxonomy.

Research into vector-borne disease calls for this broad approach because it requires a multidisciplinary understanding of how vector and pathogen interact with each other as well as the environment. That is because vectors transmit disease biologically rather than mechanically. As O’Neill explains it, “Vectors do not act as simple syringes injecting pathogens from one human to another the way a hypodermic needle might pass on AIDS or hepatitis.” Instead, they are the vital biological links that allow the pathogens to spread. Bacteria and viruses proliferate within the shelter of the vector’s body. Protozoa use the vector as a nursery where they multiply by completing a multi-stage life cycle. For example, the life cycle of the *Plasmodium* protozoan that causes malaria begins in the mosquito’s stomach, where the

protozoa multiply, and culminates in the mosquito's salivary gland. From there, *Plasmodium* parasites are passed on to a new host through the mosquito's bite. In the human, these malaria pathogens then invade the liver, causing spleen enlargement, kidney disease or malignancy.

In recent years there has been a growing awareness of the importance of the vector-pathogen interaction. Yale investigators are looking for vulnerable points in the insect at which the chain of disease transmission can be interrupted. They are looking for ways to make the vector unfriendly to the disease pathogen or, alternatively, to prevent the pathogen from maturing or multiplying within the vector. One strategy is to make use of symbiotic bacteria that normally live in a mosquito or fly. The aim is to use the bacteria to "hitchhike" in new genes that interfere with a disease pathogen's ability to multiply or to complete its life cycle within the vector. If it can't mature or multiply within a vector, the pathogen cannot infect a new host.

Although vector-borne diseases have plagued humans throughout history and, indeed, affected the fate of civilizations, the notion that they were spread by insects did not even arise until a century ago. The discoveries by Ronald Ross and Giovanni Battista Grassi in the late 1890s that malaria was transmitted by *Anopheles* mosquitoes, rather than "mal air," revolutionized epidemiology. Since then, however, the complexity of the interplay between vector and pathogen has hindered researchers seeking to block disease transmission. Humans fighting vector-borne diseases still do pretty much what they have been doing for generations: attempt to kill the vector. Spraying DDT on mosquitoes in the Solomon Islands, spraying deltamethrin on tsetse flies in Zaire or spraying malathion on mosquitoes in Queens are all based on the same strategy.

"You don't have to know much about disease-transmission mechanisms to do that," says O'Neill. The good news, he says, is that "we are at a turning point. We're understanding on a more fundamental level how these organisms interact. This information will open up new approaches to disease control."

Associate Professor Serap Aksoy, Ph.D., provides a dramatic picture of how the pace of research has accelerated since 1982, when she wrote her doctoral thesis. Her research, which looked at a single gene in an *E. coli* bacterium,

took her three years to complete. Today it would require a week. "I wouldn't even give it as a project to an undergraduate in my lab. It would be too easy," says Aksoy, a medical entomologist. "If somebody told me 20 years ago what I'd be doing now—trying to change the genome of an insect so it doesn't transmit parasites—I'd have told them it was science fiction."

The new insectary at Yale is central to the work of the vector biology group. The year-old, \$700,000 facility at the School of Public Health provides a controlled environment for the insect colonies maintained by the five principal investigators (who have come to Yale from four continents) and the 35 postdoctoral fellows, lab assistants and students who compose the vector biology group. Each chamber of the insectary is entered through a heavy, locked door and a thick screen zipped in place to contain the insects. Scientists entering and leaving the anteroom of the locked facility walk under a powerful fan designed to blow off any clinging insects.

The four-chamber, 1,200-square-foot containment laboratory is tightly monitored to maintain correct temperature and humidity; its lighting simulates the diurnal cycle. The insects here are mostly laboratory colonies whose ancestors were collected in Kenya, Mali, Thailand and India, now living in small mesh cages. The colonies in residence recently included two species of mosquitoes that can serve as malaria vectors; tsetse flies, which can carry the pathogen for African sleeping sickness; mosquitoes trapped at the Bronx Zoo to be tested for the West Nile virus; and fruit flies and moths that serve as experimental models. (Ticks, which are arthropods but not insects, live down the hall.) As a rule, the insects here are not carriers of disease, although the laboratory does have a separate chamber and a higher-level safety protocol for carriers, if needed.

In one of the humid insectary chambers on a recent morning, white-coated research associate Irene Kasumba, M.Sc., monitored a mating cage for *Glossina palpalis palpalis*, or tsetse flies. She pointed out two plump fly couples mating in the little mesh enclosure, members of the only colony of tsetse flies in North America and one of only a handful of lab colonies in the world. In the tray below them were a number of small, black pupae, the size and shape of apple seeds. Kasumba moved them to closed, aerated dishes, where they would remain until

GALE ZUCKER



"We are at a turning point," says Scott O'Neill, head of the vector biology section. "We're understanding on a more fundamental level how these organisms (vector and pathogen) interact. This information will open up new approaches to disease control."

emerging a month later. In the adjacent chamber housing mosquitoes, larvae and pupae wriggled in pans of water. Mosquito pupae ready to emerge as winged adults had graduated to little bowls of water within mesh cages.

O'Neill tells the story of a fellow graduate student back in Australia who coddled her mosquitoes by feeding them the very best blood: her own. Since some mosquitoes feed at night and are adapted to thrive on human blood, she would take the mosquitoes home, strap little mesh boxes on her arms and let them bite her while she slept. At Yale, researchers depend on hamster collaborators to supply the blood. The hamsters lie supine, anesthetized, on mesh hammocks on top of the insect cages, providing meals to the insects flying around below.

Other insects are stored in freezers upstairs. Research Scientist Leonard E. Munstermann, Ph.D., keeps frozen (and sometimes live) sand flies, the vector for the *Leishmania* protozoan. Associate Professor Fish has frozen 500 more Bronx Zoo mosquitoes that he is screening for West Nile infection. Knowing the prevalence of West Nile in last summer's mosquitoes will give public health officials some idea of what to expect this summer. In May, Fish, Munstermann and a group of public health students will collect more mosquitoes at the zoo, identifying the species and testing them for West Nile virus.

"We'll know pretty early whether the virus is going to re-emerge or not," says Fish. "We're going to have a very tight surveillance program there." If the virus does reappear, Fish recommends "source control," using fish, bacteria or insecticide to kill mosquito larvae in places like storm drains and catch basins. He has been vocal in urging lawmakers to pay attention to the dangers posed by mosquitoes, attending legislative hearings and appearing on television news programs.

Vector biologists acknowledge that eradicating vector-borne diseases may prove impossible. Each time human beings make a new attempt to defeat them, vectors and pathogens contrive to survive the assault. "I think you can expect them to adapt to most things," says O'Neill. "Evolution's a pretty powerful thing. When you're faced with extinction, it's amazing how quickly a population will respond or change for survival. It's a continual arms race with biological organisms." **YM**

TAKING AIM AT MOSQUITOES, AT THE LEVEL OF MOLECULES

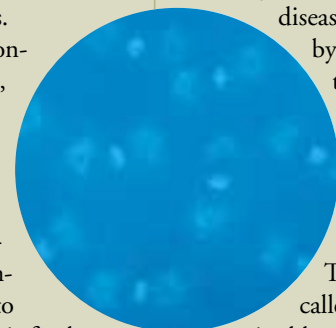
Vector biologists at the School of Public Health are developing new approaches to disease control by studying the interaction between arthropod vectors and the disease pathogens that live within them. This work is vital, says Assistant Professor Liangbiao Zheng, Ph.D., because "many vector-borne diseases are coming back with a vengeance in parts of the world." Diseases are not only re-emerging but spreading to new places, as with the West Nile virus discovered in New York City last summer.

Associate Professor Serap Aksoy, Ph.D., specializes in research on the tsetse fly, which carries the protozoan that causes trypanosomiasis, also known as African sleeping sickness. Largely under control in the 1960s, trypanosomiasis is resurgent in central and East Africa, resulting in the worst epidemic of the century, according to Aksoy. Infection is fatal to farm animals; in humans, it causes intermittent comas and kills its victims if left untreated.

Aksoy is investigating how a naturally occurring bacteri-

um that lives in the tsetse fly can be altered genetically to make the fly inhospitable to the protozoan that causes sleeping sickness. She and her lab team have managed to introduce genes into the symbiotic bacteria and to place the bacteria into the flies. They are still working on finding genes whose expression will block the parasite. Aksoy hopes that eventually "engineered" flies that resist the protozoan causing sleeping sickness can replace natural populations in the field, thus stemming the spread of illness.

Associate Professor Scott L. O'Neill, Ph.D., head of the vector biology section, is hoping to interfere with disease transmission by using a bacterial parasite found naturally in about one out of five insect species. The parasite, called *Wolbachia*, is able to actively invade field insect populations by manipulating the insects' reproduction so as to favor its own vertical transmission. This ability, together with *Wolbachia's* widespread distribution and ability to be introduced into new species in the laboratory, make it a very



THIS PAGE: SERAP AKSOY, SCOTT O'NEILL; NEXT PAGE: OLIVER MECKES / SCIENCE SOURCE; PHOTO RESEARCHERS

(continues on page 22)



OPPOSITE PAGE:
The *Wolbachia*
bacterium, bot-
tom, shows
promise as a
candidate for
genetic manip-
ulation of a
variety of
pathogens,
including *Plas-
modium*, top,
the protozoan
responsible for
malaria.

ABOVE: A pre-
cisely detailed
view of a mos-
quito and its
mouth parts
as captured by
a scanning
electron micro-
scope.



GALE ZUCKER (2)



Principal investigators in the vector biology section are, from left in top photo, Leonard Munstermann, Serap Aksoy, Durland Fish, Scott O'Neill and, with pipette above, Liangbiao Zheng.

attractive tool to manipulate the genetics of a wide spectrum of insect-disease vectors.

O'Neill is proposing to use *Wolbachia* in two different ways. The first is to harness *Wolbachia* as a vehicle to express foreign genes within mosquitoes. These genes could then be introduced into populations of mosquitoes, using *Wolbachia's* natural spreading ability. The genes of interest to be expressed by *Wolbachia* would be those that could prevent human pathogens from being successfully transmitted by the vector—for example, single-chain antibodies that target the malaria parasite within the mosquito and prevent it from invading the insect's salivary glands.

Another, simpler strategy is to utilize virulent strains of *Wolbachia* to shorten the

insect's adult life. This approach exploits the fact that pathogens typically need a lengthy period to develop in the body of the insect before they can be transmitted to another human. (In any given mosquito population, only a small fraction, the oldest insects, is responsible for the majority of disease transmission. Since these older insects contribute little to reproduction, the mosquito population remains intact, but the pathogen is eliminated.) The O'Neill lab is currently evaluating the age-shortening strategy in tsetse flies and *Aedes* mosquitoes that transmit the dengue virus. They hope to extend this work to malaria vectors in the near future.

Some *Anopheles* mosquitoes naturally resist the malaria protozoan. Zheng is exploring the genetic and molecular basis for the immune response that allows some mosquitoes to avoid infection. His group is zeroing in on the locus for the gene that determines susceptibility. Could *Anopheles* mosquitoes be bred with immunity to the malaria protozoan?

Associate Professor Durland Fish, Ph.D., in addition to his work on West Nile, has spent the past decade staking out the territory of the tiny deer tick that carries Lyme disease. Among the tools at his disposal is remote sensing data provided by NASA, allowing Fish to use satellite images and other records to predict where the risk of tick-borne disease will be highest. This information is useful in planning prevention strategies, including use of the Yale-developed Lyme disease vaccine that became available last year.

Research Scientist Leonard E. Munstermann, Ph.D., is doing basic research on sand flies, the vector for protozoa causing the two forms of

leishmaniasis. One form causes disfiguring sores on the skin; the other leads to fatal disruptions of liver and spleen function. Leishmaniasis causes between 1.5 million and 2 million new illnesses annually, according to the World Health Organization. The fatal form is epidemic in eastern Brazil. (Ironically, when insecticide programs against malaria mosquitoes are terminated, it is the sand fly population that can surge to produce the prevalent disease problem.)

A population geneticist, Munstermann is interested in whether genetically distinct sand fly populations should be reclassified as subspecies, some of which carry the protozoan, some of which don't. This would have implications for vector control; there is no need to kill subspecies that don't carry disease. He turned an informal population study of his own into an exhibit at Yale's Peabody Museum. There he has displayed over 200 insects, from mayflies to butterflies, trapped in his suburban back yard.

Munstermann is inspired not only by the possibility that he could help find a way to control the spread of leishmaniasis, but also by what the flies can tell us about all living organisms. "I'm interested in how things work. Here are flies no one has ever looked at. They're important to humans. What are they made of?"

He is drawn to his work in part because understanding how genes interact in tiny parasites and insects can provide information about human beings as well. As he says: "DNA is DNA. We're just a more complex glob of DNA attempting to understand how less complex globs of DNA interact."

WINGS OF DISEASE

Vector-borne illnesses such as malaria, Lyme disease and West Nile encephalitis rely upon secondary organisms such as mosquitoes, ticks or tsetse flies to carry the pathogen from host to host. In nearly all cases, the vector plays an essential part in the infectious agent's life cycle, in addition to being a convenient means of transportation.



VECTOR +
MOSQUITO

+ *Plasmodium spp.*
+ West Nile virus
+ Dengue virus
+ Yellow fever virus

= Malaria
= West Nile encephalitis
= Dengue and dengue hemorrhagic fever
= Yellow fever



TSETSE FLY

+ *Trypanosoma spp.*

= African sleeping sickness



SAND FLY

+ *Leishmania spp.*

= Leishmaniasis



KISSING BUG

+ *Trypanosoma cruzi*

= Chagas' disease



TICK

+ *Borrelia burgdorferi*
+ *Ehrlichia spp.*

= Lyme disease
= Ehrlichiosis

Common Vector-borne diseases



MALARIA

On the rise throughout the world, malaria is commonplace in Africa, Asia, the Middle East and Latin America. More than 300 million new infections occur each year, resulting in 2 million deaths annually. Vector: *Anopheles* species of mosquito, especially *Anopheles gambiae*.

AFRICAN TRYPANOSOMIASIS (SLEEPING SICKNESS)

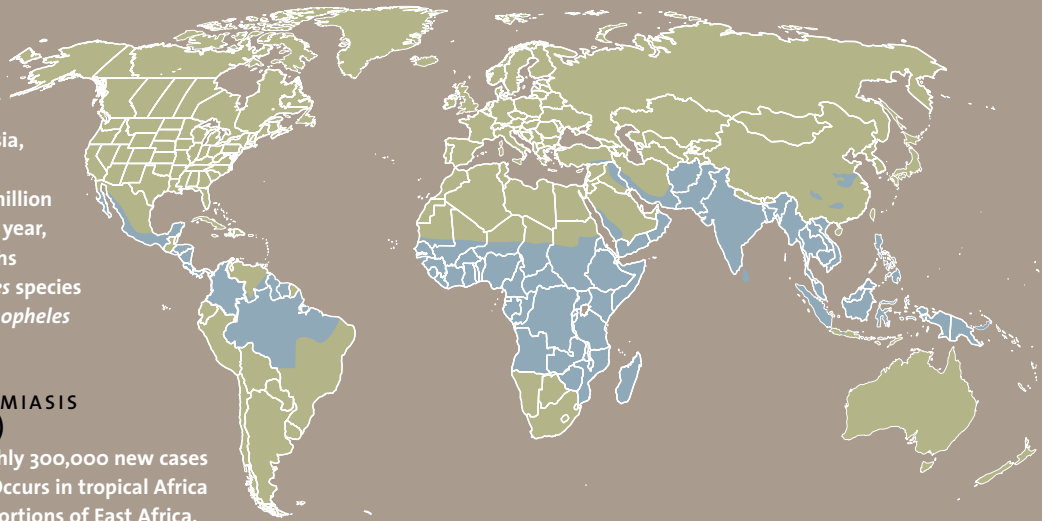
Surveillance is poor; roughly 300,000 new cases are estimated each year. Occurs in tropical Africa and at epidemic rates in portions of East Africa. Vector: tsetse fly.

DENGUE FEVER

Currently 500,000 people are hospitalized worldwide. Approximately 24,000 deaths each year. Prevalent in Africa, India, Southeast Asia, Latin America and Australia. Vector: *Aedes* species of mosquito, especially *Aedes aegypti*.

LEISHMANIASIS

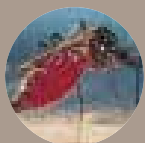
Two million new cases reported each year. Twelve million infected now. Occurs in 88 countries, chiefly in South America, the Middle East (Gulf War veterans returned home with the disease) and India. Vector: sand fly.



CHAGAS' DISEASE

Occurs only in Western Hemisphere. Widespread in Central and South America, where more than 16 million people are believed to be infected and 100 million are at risk. Vector: Various species of triatomid insects, also known as kissing bugs.

Sources: World Health Organization; Yale Vector Biology Section, Department of Epidemiology and Public Health.



A man with a beard and glasses, wearing a dark suit, white shirt, and a red and white patterned tie, is sitting in a room. He is smiling and looking towards the camera. His hands are resting on his lap. The room has dark wood paneling, a framed picture on the wall, and a large window with a diamond-patterned leaded glass design. The lighting is warm, suggesting an indoor setting with natural light from the window.

INTERVIEW

In search of medicine's shifting frontier

The forward edge of medical knowledge may be an elusive target for teachers, students and clinicians. That doesn't bother Herb Chase, the school's new deputy dean for education.

By John Curtis

Photographs by Gale Zucker

Herbert S. Chase Jr., M.D., believes in bringing medicine to what he calls “the edge,” the constantly expanding outer limit of medical knowledge or “the most detailed explanation [of a given topic] that we have right now.” It is to the edge that doctors must now turn in treating their patients, says the new deputy dean for education. And as the edge of knowledge advances with each new discovery, medical students must learn how to find and evaluate it.

It was “the edge” that brought Chase to Yale. Last April he came to the Cushing/Whitney Library to talk about the Internet as a research tool in medicine. In the audience were at least two members of the search committee for the deputy dean’s position. At the time Chase had no plans to leave Columbia University College of Physicians and Surgeons, where he has spent 22 “absolutely fabulous years” and received high honors for his teaching, including the university’s Presidential Teaching Award. The lure of spreading his vision for education across a broader canvas proved too great to resist, however. On July 1, he will formally begin his Yale duties. Until then Chase plans to visit New Haven once a week to meet with faculty and students. Chase will continue to live in New York City, where his wife is a lawyer and one of his sons is still in high school. He has another son in college.

Medical education, Chase says, has become all consuming. He used to dabble in photography and play classical guitar, bassoon and clarinet. He still goes to the opera but has little time for activities outside his work and family.

Staff Writer John Curtis visited Chase at Columbia recently. An edited transcript of their conversation follows.

What are the challenges facing medical education, around the country and at Yale?

The problem with medical school in general is that there is a language of between 15,000 and 20,000 new words that must be learned by students before they can converse with their colleagues about patients. Because of the time pressure to learn that language during the first two years of medical studies, it’s hard to weave a meaningful clinical experience early on. But clinical studies can be put into those first two years. And after that there is no reason we can’t have a more fluid integration between clinical and basic science during the third and fourth years.

One of the challenges of medical education is teaching the content at the right time. We have a pretty good view of what we need to teach. The problem is finding the right spot. We often teach genetics concepts in the first year, which is appropriate. Then we teach abnormal genetic makeup in the second year, and that is more suitable to the third and fourth year. A good deal of the basic science would be much more interesting to the student in the third or fourth year.

Most medical schools are behind electronically. Say you’re a patient and I’m your doctor. I have core knowledge, which allows me to figure out what you’ve got. It also allows me to find information in the library. Now my role is not to look into my brain and see what’s up there. That’s ludicrous. That’s likely to reveal old information. I go to electronic search engines right here at my fingertips. Finding the edge is a skill. Assessing the edge is a skill. Medical students must be provided adequate computing facilities. The curriculum must demand that they use computers. >>>

At Columbia, you directed interdisciplinary basic science courses for first-year students. Do you plan to encourage similar courses at Yale?

It's definitely on the table at many places. The basic principle—that basic science activities are confined to the first couple of years and clinical activities are confined to the third and fourth years—all emanated from the Flexner Report [of 1910]. I think that paradigm is no longer valid. There's nothing preventing us from having a much more fluid curriculum, where we have basic science and clinical science interwoven throughout the four years.

For a long time, the national boards were given in June of the second year. There was no compelling reason to have the students start the clinical years in March, April or May because their minds would not be on the task. That's all changed. You can hook up online and make a date to take the boards in January. That alone, as absurd as it may sound, may be the linchpin of the whole reorganization nationwide in terms of fully integrating medical education—starting the clerkships earlier, starting the clinical material earlier and then bringing basic science into the clinical years.

“There’s nothing preventing us from having a much more fluid curriculum, where we have basic science and clinical science interwoven throughout the four years.”

Traditionally, departments have determined course content. How do you secure departmental cooperation in integrating courses?

Departments have a legitimate stake in the pedagogical process in terms of imprinting their vision of biology on the student. That is a very powerful vision. It should not be lost. An integrated course does not minimize that vision. In fact, it strengthens that vision. The individual disciplines maintain their identity by providing an essential piece to the mosaic which creates a vision of the patient as a whole entity. Departmental identity is also established and reinforced in problem-solving sessions that are central to an integrated presentation of human biology.

The departments also play a critical role in helping the student develop medical decision-making skills. Why do we teach basic science? We obviously teach basic science so we know the molecules of the body and how they work. But there's a much more important lesson from basic science, one that is long-lasting. We teach basic science so that the student learns the scientific method and how to apply the scientific method at the bedside. Yale has a leg up on everyone because it has the thesis. This, in spades, gets the student up to speed in terms of analyzing and assessing data.

We need to divide the curriculum into two equally important units. One is content. You cannot proceed in medicine without a core of knowledge. A second, equally important goal is to provide process, to find ways for the student to master the scientific method.

How can technology help us gain access to the latest knowledge derived from advances in research at the molecular level and the mapping of the human genome?

We will reach a state where we will know every molecule in the human body. It is likely that we will know from a drop of blood that a patient has 14 of 19 genes for high blood pressure and we have 172 drugs that will interact with that. Only a computer will be able to organize this information. This, of course, poses a difficult challenge. The physician must be skilled at complex decision-making. The doctor's role will now be one of judgment, where we look up the information on the patient, who is alive and breathing next to us, and we make an appropriate decision. Technology is creating the need for a rigorous medical decision-making curriculum. That does not exist in any medical school curriculum and Yale can lead this effort.

How do you educate physicians to become more than technicians, and how do you ensure that they treat the patient, not just the disease?

The medical school curriculum in general—and this is true nationwide—is one of deconstruction. The patient comes in and we look at the biochemistry, we look at molecules, we look at the organs. We have little pieces of the patient that we pull apart so we can study them. Then a process of reconstruction has to occur. That is what I think is lacking in medical schools.

Graduates leave medical school feeling comfortable with part of the patient rather than the whole patient. If you come to me with heart disease, am I more likely to give you a medicine than send you for an operation because I am an internist? If you go to a surgeon are you more likely to be operated on than receive medicine? Activities that focus on the whole patient need to be built into the curriculum. Yale has this fantastic new elective called “Women’s Health.” It’s very successful. The focus is on the person. Yale could devise a number of short, meaningful whole-patient views of medicine.

Integration of the basic sciences reinforces the whole-patient view as well. If one studies only the physiology of the system or the cell biology of the system, we are deconstructing. We could reconstruct these disciplines into a functional view of the whole patient as we rotate through the body.

How can you instill in the faculty the notion that teaching, as well as clinical or research excellence, is a path to recognition and advancement?

Teaching needs to be rewarded. There has to be daily recognition from the University that you are doing a great job. Those of us who are deeply committed do it for the satisfaction we get. At our level of teaching, yes, it is very important to serve as a role model to excite the students about what we do. That is the real skill of the charismatic teacher. Nevertheless, the University must recognize and encourage outstanding teaching.

We need to define the career path for teachers. Who will lead the educational programs when we all retire? Faculty development of great educators is as important as the development of great scientists and clinicians. Yale has created a clinician-educator track and that is a major step forward. This will guarantee that Yale remains one of the great medical universities in the world. **YM**

“It is likely that we will know from a drop of blood that a patient has 14 of 19 genes for high blood pressure and we have 172 drugs that will interact with that. Only a computer will be able to organize this information.”



Chase and research librarian Charles Greenberg, left, talk with students in the Cushing/Whitney Medical Library. “Technology,” Chase says, “is creating the need for a rigorous medical decision-making curriculum. That does not exist in any medical school curriculum and Yale can lead this effort.”

TEACHING

Deconstructing



education

The breathtaking discoveries of the last three decades and rapid change across all of medicine have called traditional models of medical education into question. At Yale, the debate is in full swing. **By John Curtis**

The school was at a crossroad. Medical knowledge was growing at a startling pace. Wondrous new cures were in the making, and scientists were beginning to understand the complex workings of disease at a level of detail that was unprecedented. As a result, medical students had to master a stupefying mass of knowledge. A new way of teaching was needed.

The time was 1922. The dean was Milton Winternitz, M.D. His solution was the Yale System of medical education. Eight decades later, students and faculty face similar problems—masses of new findings about disease and treatments and overwhelming amounts of knowledge to be learned, compounded by the escalating speed of discovery and communications. Add to the mix changes in the economics of medicine and delivery of care, and what you have is a medical school at a crossroad, once again contemplating precisely what, and how, to teach.

“Yale medical students love the Yale School of Medicine,” says immunologist Charles A. Janeway, M.D., “but they don’t love everything about a Yale medical education.”

What’s not to love? Of the 3,500 applicants seeking a place in next year’s entering class, only 105 will be given the opportunity to study medicine here with more than 1,000 of the world’s most highly regarded clinicians and basic scientists. The school’s pioneering laboratories churn out new discoveries about life at the molecular level at an astonishing rate. Articles by faculty appear almost daily in prestigious medical and scientific journals. Students learn from physicians at one of the nation’s top teaching hospitals. During the fall term this academic year, the school saw guest lectures by two Nobel laureates, one of the leading lights in gene therapy, and a slew of distinguished visitors from around the world.

Then there is the Yale System of medical education, a unique approach to learning that remains strong after three-quarters of a century. Its elements—time for independent study, no grades or class rankings, treatment of students as mature adults responsible for their education—all add up to a unique atmosphere. For one thing, says fourth-year student Evelyn Duvivier, “We’re not competing against one another. This is an environment where the focus is on learning. Students are driven by knowledge, not by grades.”

With all this, in the view of many students and faculty, it’s still time for a change. Janeway, a professor of immunobiology and biology, is in a position to know. Since early last year, he and Ralph I. Horwitz, M.D., chair of the Department of Internal Medicine, have led an education committee convened by Dean David A. Kessler, M.D., with an eye to



Jan. 3, 2000, third-floor anatomy laboratory. Sterling Hall of Medicine. As is tradition, students of anatomy become familiar with every inch of the body during the first year of their medical education. **At left**, professor William Stewart leads three students in a minute exploration of the lungs as a second group, **above**, examines X-rays in preparation for their time with the cadaver.

PHOTO ESSAY: A CLOSER LOOK AT TEACHING PHOTOGRAPHS BY JOHN CURTIS

For much of the past year, a committee of faculty, students and administrators has taken an exhaustive look at medical education at Yale, to ensure that teaching is as good as it can be and that Yale remains at the forefront of medical schools internationally.

Of the many questions guiding the process, two are key: “What does a 21st-century physician need to know?” and “How should we teach it?”

As the dean’s committee on medical education looked to the future, Staff Writer John Curtis

went into classrooms, laboratories and clinical floors to take a closer look at teaching as it occurs day in and day out. During the course of several months, he photographed students in many of the situations that comprise a Yale medical student’s educa-

tion—from the first up-close view of human anatomy to the development of clinical skills with patients and colleagues. Here and on the pages that follow are photographs that document important elements of a Yale medical education.



Jan. 3, 2000, third-floor anatomy laboratory, Sterling Hall of Medicine. Students work in teams of three or four as they learn to identify the thousands of nerves, tissues, muscles and organs that make up the human body. The course starts with an orientation to prepare students for their own reactions to dissecting a human body and ends with a ceremony honoring those who gave their bodies to medicine. (While Yale is a leader in comput-

er-based teaching, it remains committed to the use of cadavers for anatomy instruction.) **Top right,** Professor Shanta Kapadia helps a group of students understand the geography of the lungs at one table. **Above,** first-year student Marta Rivera and two classmates probe the lungs at another table while across the hall, students are engaged in a similar exercise.

improving the curriculum as well as the school's more general approach to education. Not all of the committee's recommendations are new. Each decade since the 1920s, previous committees have made proposals on various facets of the educational experience without always seeing them implemented. But there is a sense this time that things are different.

"There are both internal and external forces demanding a revision of the curriculum," says Ashgar Rastegar, M.D., a professor of medicine and member of the education committee. "There has been a major revolution in science. There has been a major revolution in the delivery of care. Society is demanding that we look at whether we are training the right kind of physicians. Students and faculty are asking, 'Is this the best way to teach and to train physicians?'"

"There is change occurring everywhere we look," says committee co-chair Horwitz, "not only in the health care system in which we practice, but in the medical schools that are our peers."

The committee's charge, in the words of Kessler, was to inquire into "what we teach and how we teach." The consensus of its members, after meetings with course directors, faculty members and students, and reviews of curricula at other medical schools, was that medical education at Yale is very good but could be better. As its guiding principles, the committee proposes to enhance the educational environment, refocus the educational process, strengthen the Yale System, enrich the

John Curtis is a staff writer for Yale Medicine.

curriculum, redesign administrative oversight and implement new programs in medical informatics. Last fall it presented a list of initial findings to department chairs and the faculty. As *Yale Medicine* went to press, school-wide discussion of the issues raised by the committees was beginning in earnest. Kessler, who has not endorsed any specifics of the plan so far but supports the direction of the committee, has held several meetings on the topic with the department chairs. A series of "town meetings" with faculty and students, begun in January, was to continue through the spring.

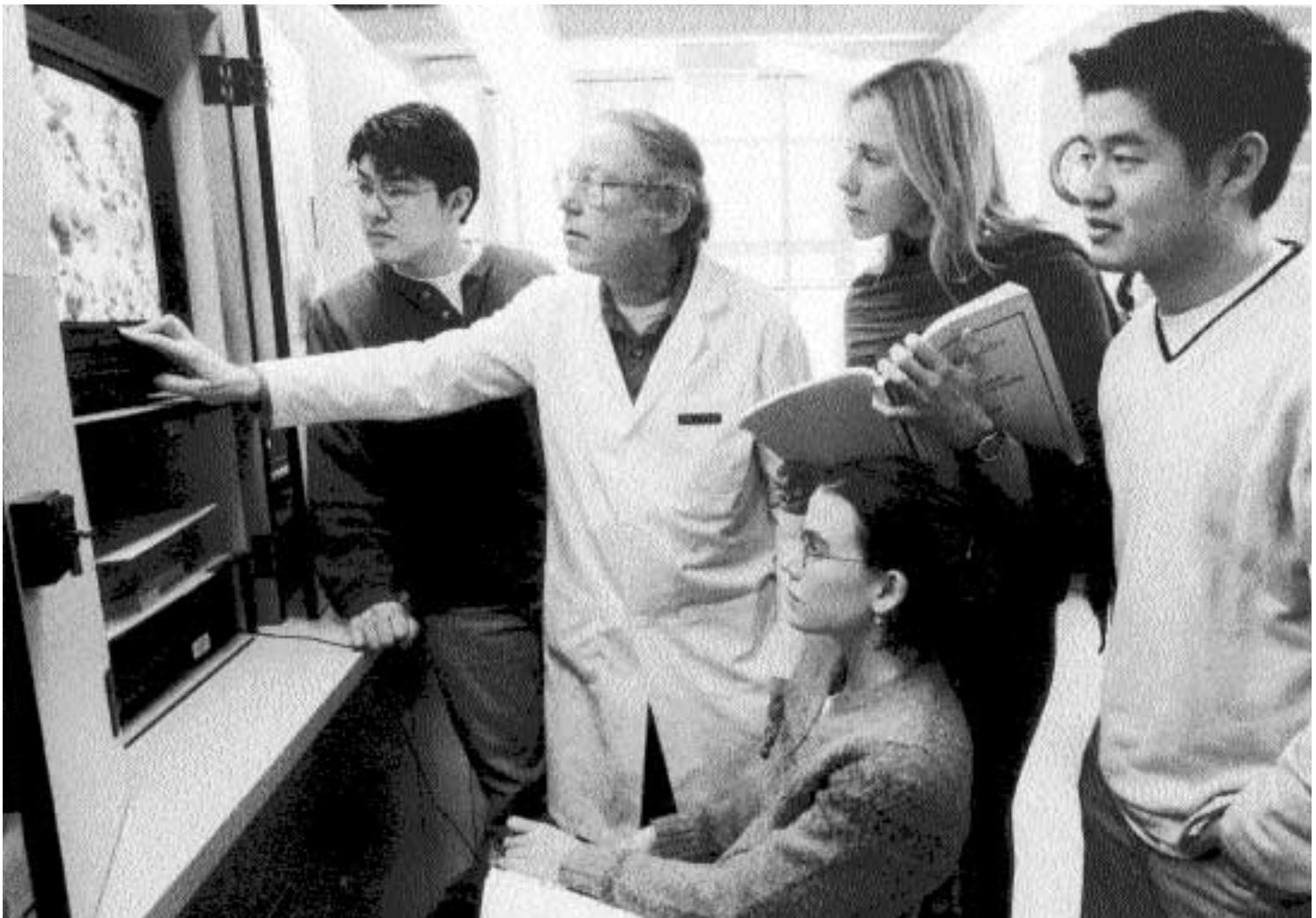
"Yale School of Medicine," says Horwitz, "is trying to find a way, given the extraordinary changes taking place in medicine, to renew the Yale System's fundamental principles— independence, self-study, understanding the scientific method and applying science-based medicine to clinical problems." When Winternitz introduced the Yale System in the 1920s, he eliminated 1,200 hours of instruction from the schedule. The crushing burden of the curriculum, he felt, stifled independent study, contemplation and initiative. Advocates of the Yale System felt that absorbing a mass of facts was less important than a grounding

in fundamental principles, methods of investigation and the scientific method.

Now the education committee's goals are to integrate course materials across departmental boundaries, implement more case-based teaching, correlate the basic and clinical sciences, allow students more structured time to conduct original research toward their thesis requirement, cut down on class hours, and restructure the program so that clinical studies begin on the first day of medical school and basic sciences continue to the last day. Clinical exposure in the first two years, the committee found, is insufficient and haphazard, and the third-year clerkships need a thorough review. Some peer institutions have already tackled these issues, Janeway and Horwitz note, and are moving toward a system of problem-based learning and small-group teaching, rather than large lectures.

The committee also addressed the prevailing notion among the faculty that the road to recognition, advancement and tenure lies not in teaching, but in research and clinical work. "Nothing," says Janeway, "undermines the success of medical education more than the perception that teaching is secondary." >>>

Feb. 8, 2000, histology laboratory, Lauder Hall. A month after their introduction to the lungs in the anatomy laboratory, first-year students continue their study of the pulmonary system under the tutelage of cell biology professor Thomas Lentz. Looking through the microscope and at histology slides enlarged on a computer monitor, the students learned about the lungs at the cellular level.





Nov. 4, 1999, seminar room, Sterling Hall of Medicine. Emile Boulpaep, professor of physiology, talks about chemical processes and their biological consequences during a seminar for first-year students.



Dec. 14, 1999, Room 110, Jane Ellen Hope Building. In the semester's final lecture in microbiology, second-year students learn about the practical aspects of treating viruses, including common childhood ailments.

In presenting their findings, Janeway and Horwitz made it clear they're under no illusions about the complexity of their task. Making changes means placing authority for curriculum in the hands of the deputy dean for education, who, under their proposal, would be armed with a sizeable budget. The new deputy dean, Herbert S. Chase, M.D., was chosen in part because of his experience in curriculum design. At the Columbia University College of Physicians and Surgeons, where he has taught for 22 years, he created courses that integrate basic and clinical sciences. He's also very interested in applying information technology to medicine, to ensure that physicians have the best possible data when they're treating patients. Chase, currently a professor of clinical medicine at Columbia, will officially begin his duties at Yale in July. One of his first, and most important, charges is to oversee the curriculum revision process. "We live in an era in which we can easily discuss the molecular basis and the molecular treatment of very common diseases," says Chase. (See Interview, page 24)

"They really go hand in hand. There's nothing preventing us from having a much more fluid curriculum where we have basic science and clinical science interwoven throughout the four years."

Past efforts at curriculum reform have generally stumbled over departmental turf battles. "The curriculum too often finds itself responding to the needs of the department rather than what might be pedagogically sound," says Robert H. Gifford, M.D., HS '67, who served as the school's

first deputy dean for education until his retirement in December. "It has been very difficult to convince basic science departments to reduce class hours, to introduce interdepartmental teaching, to introduce case-based teaching and to form partnerships with clinical faculty."

Emile L. Boulpaep, M.D., professor of cellular and molecular physiology and the department's interim chair, headed a curriculum committee a decade ago but found departmental and faculty resistance to reform too strong to overcome. "It touches on very special issues of identity," he says. Frustrated in his attempts to forge wider interdepartmental integration and coordination, he and col-

league James D. Jamieson, M.D., Ph.D., head of cell biology courses, did it themselves on a smaller scale. Physiology and cell biology are still separate courses, but lectures and classes are scheduled to complement, rather than repeat, each other. “We are here to make the optimal learning process for the students,” says Boulpaep. “If that learning process requires working together and integrating two fields of science and the student will reap the benefit of it, there is no reason we shouldn’t do it.”

There are other examples of integration. Second-year students take a course called “Mechanisms of Disease,” which takes a system- and organ-based approach to material traditionally taught in pathology, pharmacology, laboratory medicine and other disciplines. But some faculty would like to see much more collaboration. Jamieson, who won the 1999 Bohmfalk Prize for excellence in basic science teaching, believes the basic core of what physicians must know hasn’t changed. “They need to have a solid grounding in cell biology, molecular genetics, pharmacology, physiology, biochemistry and pathology. You can’t be a doctor without those things,” he says before adding: “There is a lot of stuff that could be cut out if courses were better scheduled or better integrated.” Jamieson also stressed that as the number of students in the M.D./Ph.D. program increases from about 10 percent of the class to 15 percent, the school must continue to emphasize a solid foundation in the basic sciences that will be required of physician-scientists.

In the classrooms along Cedar Street, faculty members employ a number of teaching approaches. Some classes follow a traditional undergraduate model of a large lecture followed by small-group meetings with a graduate student. Boulpaep prefers the small groups of about 10 students he convenes every Thursday morning for lessons in physiology. He uses the Socratic method, tossing out questions, then questioning the answers. “Why would the blood not be saturated?” Boulpaep asked of a case of cystic fibrosis. “It’s not getting oxygen,” a student responded. “Why is it not getting oxygen?” Boulpaep asked, prodding the students.

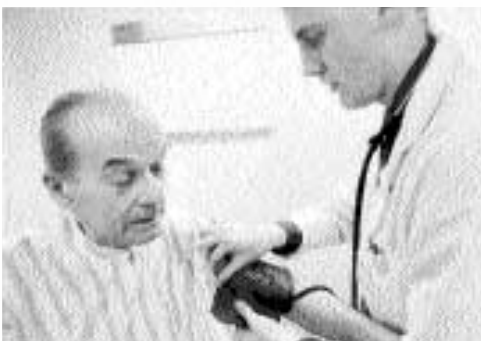
Across campus at the Yale Health Plan, medical student Duvivier, then in her third year, worked one-on-one with a physician-supervisor in internal medicine as part of her clinical clerkship. Typically, she would interview patients on her own, then present her findings and diagnosis to her supervisor. One



Feb. 4, 2000, clinical skills assessment lab, Farmington, Conn.

During the second year, students prepare for the transition to full-time clinical studies. As they have for the last two years, a group of Yale medical students makes the 40-mile trek to the University of Connecticut Health Center, where they are paired with “patient-instructors” who play the role of patients and drop clues intended to lead students to a correct diagnosis. Only a handful of medical schools have developed assessment labs as sophisticated as the

UConn program, which is housed in a former ob-gyn clinic with 12 examination rooms. The history and physical exam are observed, videotaped and evaluated, giving the students an opportunity to get comfortable in the clinical setting and learn from their mistakes. **Above and below:** Kier Ecklund interviews one of the patient-instructors under the watchful eye of a video camera on the wall.



case involved a 63-year-old police officer with a cough. Duvivier reported to David Smith, M.D., her suspicion that the officer was reacting to the dander of a cat he'd acquired a month earlier. "I think it is very hard for someone to acknowledge that their symptoms might be caused by something they treasure," Duvivier said.

"It sounds very classic, doesn't it?" Smith asked. "I think you did a very good presentation formulation. Do you think we need to do any further work-up for the cough, a chest X-ray?" Smith wanted to rule out tuberculosis, a risk of the officer's job. "You're right," Duvivier said. "A PPD skin test and a chest X-ray would rule that in or out."

When it works, education in the clinical years is satisfying to those involved. "I feel that my opinion and my diagnosis are taken very seriously," Duvivier says. "I'm still a student, but I am treated almost as a colleague."

That said, students and faculty have their gripes. Faculty complain about students who don't show up for lectures and small-group seminars. Students cite examples of attendings who miss rounds. And there's the evaluation system during the clinical years. "It is not based on anything scientific," says Janeway. "It is based on residents liking you or not liking you."

Medical education throughout the country has its roots in the 1910 Flexner Report. Concerned about the rise of proprietary schools that were thought to be little more than diploma mills, the American Medical Association commissioned a study by Abraham Flexner, a noted education reformer. He took as his model Johns Hopkins in

Baltimore, where the medical school was affiliated with a university and had a strong research component. Since then medical schools have, by and large, followed the same pattern—two years of basic sciences followed by two years of clinical studies. After the Flexner Report, the next big change in Yale medical education came in 1922, when Winternitz and his faculty began to implement the Yale System. Faculty kept an eye on the system, monitoring it through the 1930s and 1940s. Despite some tinkering with its elements, it has survived largely intact over the years.

"What is good about the Yale System is the collegial atmosphere," says David Spiegel, an M.D./Ph.D. candidate and one of three student members of the education committee, "and the genuine proximity students have to faculty, especially in the basic science years." Says second-year student and committee member Rebekah Gross, "It is much more humane in the sense that if you have a personal problem or something going on with your family and you can't learn something this week, then you can learn it next week. That is important in helping you stay focused."

Within weeks of donning their white coats, first-year students get a glimpse of how things could improve. "The education we get is great," says Spiegel, "but it really could be made a lot more pleasant and a lot better if there were more coordination among departments and faculty members." During his first year of medical school four years ago, Spiegel says, students faced a parade of basic science lectures that often were redundant. The result? Overlap in material, boredom on the part of students and frustration on the part of faculty who wondered why attendance was low.

How do students handle the sometimes overwhelming volume of information they must master? "You know what you should be reading and you just can't do it," says Gross. "So you pick and choose. The two words you hear most here are 'high-yield.'" That's student jargon for quality information that covers a variety of situations. The highest praise students accord professors is to say their lectures are "high-yield." Said one second-year student

Feb. 14, 2000, Yale-New Haven Hospital. Students advance their clinical skills in the second year with a doctor-patient encounter course. Andrew Norden, John Koo and Eileen Scully present cases to Howard Levitin, their clinical tutor. Teaching in the course depends on such sessions with clinical tutors, each of whom works with four students.



in praise of a lecturer in microbiology, “She tells you what you need to know.”

More integrated courses and more correlation of the basic sciences to clinical practice would ease the absorption of all that material, according to some faculty. “You don’t learn medicine by reading a textbook,” says Barry J. Wu, M.D., an assistant clinical professor of medicine and recipient of the 1999 Blake Award and the 1999 Bohmfalk Prize for excellence in clinical teaching. “You learn by seeing a patient with a particular disease and going to the textbook and reading about it. Then you have a connection in your brain.” Correlation of the basic to the clinical sciences is one of the goals of the curriculum review. It’s also the impetus behind starting clinical sciences early and continuing basic sciences until the end of the four-year program.

While all involved in teaching support the goal of improving the framework for education, the debate over how to do that is just beginning. “There’s a concern,” says Jon Morrow, M.D., Ph.D., chair of the Department of Pathology, “that the time for basic science is contracting at the same time that the knowledge base is exploding. One could argue that it would be better to go in the opposite direction and increase the hours for basic science.” Chase notes that although time allotted to basic science might be reduced in the first two years, students will return to those subjects during their clinical years. “Some basic science topics will be a great deal more compelling when taught later on in the curriculum,” Chase says.

That Yale’s medical curriculum needs some revision is no blemish on the way the school teaches physicians. As Dean Vernon W. Lippard, M.D., noted in 1954, “No educational program worth its salt ever has or ever will be in final form. To be effective, it must be subjected to constant evaluation and improvement.” The “New Curriculum” that emerged 14 years later included features current proponents of revision would recognize—reduction in basic science class hours, early introduction of students to clinical medicine, study of basic science after clinical clerkships and an extended outpatient clinical experience.

As the school stands at a crossroad, it has embarked on a dialogue about how and what



to teach doctors. Over the winter, the education committee launched its series of “town meetings” to open discussion to a spectrum of stakeholders at the medical school—faculty, staff and students. At the first of these meetings in January, Horwitz outlined different scenarios for reconfiguring the curriculum. The discussion is expected to last for some time. “Our strategy from the very beginning,” says Kessler, “was to have this committee be a several-year effort.” The committee’s proposals, Janeway notes, are designed to focus the conversation that will follow. “We need to have the whole school come together over this,” he says. [YM](#)

Jan. 18, 2000, Primary Care Clinic. In their third and fourth years, students gain more independence. They interview and examine patients on their own, then report to their supervising physicians. **Top:** During an elective in women’s health, fourth-year student Patricia Moore describes a patient’s rash to Stanley Lavietes and Rebecca Brienza. Brienza diagnoses psoriasis and suggests a treatment. **Above:** Her interview and exam complete, Moore writes up her notes in the patient’s chart. Like her father and sister before her, Moore plans to go into obstetrics and gynecology.

REMINISCENCE

Eight decades of

Dean Milton Winternitz (top) introduced the Yale System in the 1920s. By the time the Class of 1948 (above) and the Class of 1943 (right) graduated, this approach to medical education had become a tradition at Yale.

PHOTOGRAPHS COURTESY CUSHING/WHITNEY MEDICAL LIBRARY

Ever since its implementation in the 1920s, the Yale System of medical education has been the point of common reference for alumni of the School of Medicine. Ralph I. Horwitz, M.D., chair of the Department of Internal Medicine, touched on its enduring qualities when he addressed faculty recently about the education-review process now under way. “I have not been able to find two people able to agree on exactly what the Yale System is, but there is a strong consensus on the essentials,” he said. It’s an approach to learning that is self-directed and collaborative, rather than competitive. The environment is that of a graduate school. Examinations are for self-assessment, not for grades or class ranking. Learning takes place in small groups rather than in large lectures. And the curriculum should allow free time for reading, independent research and reflection.

Alumni have their own memories of how the Yale System shaped their careers in medicine. As the medical school takes an exceptionally thorough look at both how and what it teaches—all in the context of renewing the Yale System—we invited alumni to reminisce about what it meant to them. Their recollections follow.

the Yale System

A CONVERSATION THAT RESOUNDED DURING FOUR DECADES OF PRACTICE

Morris A. Wessel, M.D. '43

My most striking memory as a medical student from 1939 to 1943 is of the availability of faculty members when a student sought help. As a third-year student, I was frustrated at my inability to comfort an 8-year-old child in a cast with a fractured femur.

I went to Dr. Edith Jackson in the pediatrics department, who was interested in children’s behavior during hospitalization and had returned recently from a six-year leave of absence spent in Vienna obtaining psychoanalytic training. I remember her warm greeting as I entered her office. I shared my frustration about my patient—and remember suddenly describing bitter memories of my own tonsillectomy at the age of 8!

Dr. Jackson showed me the Anna Freud-Dorothy Burlingham studies describing the behavior of children evacuated to the countryside from war-torn London. She offered to meet with me periodically to discuss these reports and my concerns about patients.

These discussions led me to comprehend infant and child behavior in normal and stressful times. I applied this knowl-

edge during every patient contact in my four decades of pediatric practice in New Haven. I appreciate having been introduced to this explanation of children’s behavior in my discussion with Dr. Jackson 58 years ago in the Department of Pediatrics.

Wessel cared for generations of New Haven children as a pediatrician in practice from 1951 until his retirement in 1993.

PROXIMITY WAS EVERYTHING FOR A ONCE-SHY STUDENT

Richard W. Breck, M.D. '45M

The Yale System meant everything to this lecture-hall introvert. The WWII years of 1942-45 provided an exciting background in which to study medicine. The small-group instruction, either bedside or seminar, was the best part of the system for me. On rounds, standing inches from Drs. Blake, Peters, Powers, Geiger, Blumer and Tileston, I was in their debt; somehow, a bit of their intellectual dandruff fell on me and stuck.

I didn’t know the words “role model” then, but Francis Blake was, to me, the clinician I wanted most to emulate. I have been guided many times since graduating 54 years ago

by thinking, “What would Dean Blake have done in a situation like this?”

I also “mourned” the passing of the smaller classes—I think 100 is too large for YSM.

Breck, a long-time participant in alumni affairs and former secretary of the AYAM Executive Committee, retired from general practice in 1995. He lives in Wallingford, Conn., where he sees geriatric patients on a part-time basis.

‘THEY TREATED US AS RESPONSIBLE ADULTS’

Laura White Neville, M.D. '46

The one major facet of Yale’s approach to medical education that impressed me was the way they treated us as responsible adults. We were told in the first week that we had *all* been selected with the confidence that we would *all* graduate. We were told that we were capable of studying on our own, taking only those tests we wished to take, except for Parts I, II and III of the national boards. The faculty would be available for counsel and for whatever help *we* thought necessary, and without outside pressure.

I can still visualize our neuroanatomy professor as he stood at the blackboard, chalking an outline of the brain, using both hands to draw the left and right sides of the brain simultaneously. He turned to us and said, “Ladies and gentlemen, you are now members of a learned profession, and you will be students for the rest of your lives.”

Neville was in private practice in pediatrics and psychiatry for many years in Syracuse, N.Y., where she served on the clinical faculty of the SUNY Health Sciences Center. She and her husband, John F. Neville Jr., M.D. '46, are retired and living in Cotuit, Mass.

A TRUE UNIVERSITY APPROACH THAT FOSTERED INDEPENDENCE

Olive E. Pitkin, M.D. '47

Coming from a small-town high school in which most of what I learned was outside of school hours, and from Bennington College, which left its students pretty much on their own as well, I found the Yale System entirely congenial. We were offered the best of lectures, but as I became aware that I learned little from material I only heard, and that no one seemed to mind if I stayed away and concentrated on what was in the books, I was able to study in my own way with a clear conscience. In the clinical years we saw superlative physicians in action, and my images of most of them, more than 50 years later, are so vivid and still so admirable that I think we must have been given very generous exposure to these splendid role models. From them I really did learn what it means to be a good doctor. These experiences I did not stay away from; such apprenticeship can only be achieved by personal contact with a master.

If by the Yale System it is meant this true university approach—treating the students as adults who are there to

learn, making available to them the ingredients of a superb professional training, allowing them to take it in at their own pace and with techniques of their own devising—then it worked for me. My medical education has been, ever since, a matter for both gratitude and pride.

Pitkin retired in 1984 from the New York City Department of Health, where she was assistant commissioner for maternal and child health services. She lives in Westerly, R.I.

ANOTHER VIEW OF THE THESIS REQUIREMENT

David E. Morton, M.D. '48, HS '55

Having been a medical student, instructor in anatomy, and house officer at the School of Medicine in the 1940s and '50s, I had considerable experience with the thesis requirement. I also received the Keese prize for the best thesis in 1948.

Although times have changed, I concluded when I left the School of Medicine that the thesis requirement should be dropped except for those taking the combined M.D. and Ph.D. programs. My reasoning was that the thesis was truly useful only for those students planning to enter academic medicine and research. And in my day only 5 to 10 percent of the class did so. I then felt that the considerable amount of time spent on the thesis would be better spent in the study of medicine. The volume of knowledge at that time seemed so great to cover in four years without spending time on a thesis, and think how much greater it is now!

Morton, who retired from private practice in internal medicine in 1993, lives in Pueblo, Colo.

A GOOD PLACE TO BE IN THE TURBULENT 1960S

Ralph Falkenstein, M.D. '69

Historians have described the decade of the 1960s as one of turbulence and upheaval among America’s youth. Beyond the cauldron of student protests, the Vietnam War and drug experimentation, there was a haven where those fortunate enough to gain admission to the Yale School of Medicine could achieve their goal of obtaining the finest education under the relatively tranquil canopy of the Yale System.

As a member of the Class of 1969, I remain appreciative of Yale’s approach of allowing students latitude in balancing their interests and scientific pursuits with personal responsibility for absorbing course work through the guidance of concerned mentors who impart their knowledge and skills in a non-intimidating fashion. We were, at a rather tender age and with limited medical familiarity, considered responsible individuals, whose desire for learning was nurtured as thoughtfully as our hopes for developing into worthy physicians. In short, a dignified way to study a noble profession and a stark contrast to much of what was going on in the medical and nonmedical world around us.

Falkenstein is an ophthalmologist in Danbury, Conn.



'AN IDEAL EDUCATION' THAT EMPHASIZED RESPONSIBILITY

Mary Lake Polan, M.D. '75, Ph.D. '70

As someone brought up in the 1960s, the Yale System was a natural and very comfortable extension of the '60s sense of freedom and exploration. I graduated from Yale School of Medicine in 1975, having received my Ph.D. from Yale in molecular biophysics and biochemistry five years earlier. At the time I was in medical school, there were no grades and to graduate only required passing the boards and submitting a thesis. The system allowed me, during my first year of medical school, to continue working in a laboratory in the biology department, where I had been a postdoctoral fellow. I was paying for my education and Yale gave me the ability to learn and to structure that education in a way that was best for me.

Because I had a Ph.D. and did not need to submit a thesis, the Yale System allowed me to read a book on pharmacology and take Part I of the boards before my class actually had the pharmacology course. Passing the boards that first year meant I could finish medical school in three years. I wanted to learn about how medicine was practiced in other countries and the Yale System allowed me to spend both my pediatric and obstetrics and gynecology rotations at Oxford.

The Yale System stressed freedom of choice in how you could educate yourself and along with that went the personal responsibility for doing it. My experience at Yale was that everyone in both the medical school and the graduate school was available to help with research, information, advice and mentoring. All you had to do was ask. It was an ideal education that taught not just the particulars of medicine, but allowed one to live through the process of real-life decision-making and responsibility—probably the very best preparation for a career in medicine.

Polan is chair of the Department of Gynecology and Obstetrics at Stanford.

A CHANCE TO BE SELF-MOTIVATED AND REWARDED WITH KNOWLEDGE

Thomas J. Smith, M.D. '78

The Yale System is why I came to Yale in 1974 and spent \$10,000 a year more than to go to Ohio State. The flexibility of a fifth year, which happened to be free, was also a major draw.

The Yale System offered an opportunity to be self-motivated and rewarded with new knowledge (whatever its relevance) rather than punished for not knowing the answer to multiple-choice questions. The skills I honed during my time at Yale—going to the library, asking questions, not being satisfied until I knew the material and the relevant answers—have served me well in my practice and academic careers.

In addition, the thought that “Well, now I know it all and can stop studying” never crossed our minds.

As we move into a system that can track medical outcomes, and compare us one to another based on our outcomes, adherence to “best medical practice” and the subsequent good medical results will become increasingly important. Since medical care advances, the only ones who will be able to keep up are those with a “Yale System” approach of adult, life-long learning.

Smith is an associate professor of medicine and health administration at the Medical College of Virginia/Virginia Commonwealth University in Richmond.

TOOLS TO DEAL WITH A WORLD OF AMBIGUITY

Joann Bodurtha, M.D. '79, M.P.H. '79

What did the Yale System mean to me? It enabled me to get a firm foundation for life-long learning and adaptation to uncertainty. It gave us the freedom to take the time to understand something as well as it was currently understood with thoughtful teachers, small group discussion, and no preoccupation with “what’s on the test?” The memorable moments and experiences—announcement of the Nobel Prize in class, the chaplain in anatomy, a women-in-medicine lectureship, the thesis, a certain bike-riding dean’s report of prostate discomfort, and many others—continue to provide ingredients for my current clinical care and teaching.

Much of my happiness as a physician is due to the ongoing push to integrate all that medicine presents, from “marketing” public health to explaining molecular testing to a family. My Yale teachers inspired me to try to do my best with humor and caring and to learn from my mistakes.

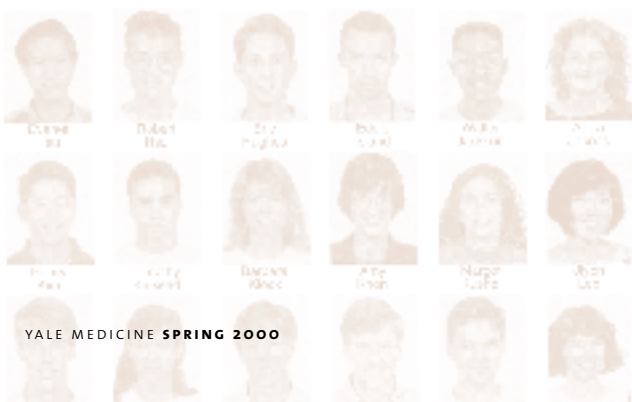
Bodurtha is an associate professor of human genetics, pediatrics and obstetrics/gynecology at the Medical College of Virginia/Virginia Commonwealth University in Richmond.

THE YALE SYSTEM PERSONIFIED

Brian B. Adams, M.D. '95

One can sum up the strength of the Yale System and the essential threads of Yale’s approach to medical education in two resounding words—Dr. Gifford.

Adams is an assistant professor of dermatology at the University of Cincinnati School of Medicine and director of dermatology at the Veterans Hospital Medical Center in Cincinnati. YM



FACULTY NEWS



JOHN CURTIS

Farewell to 'The Giff'

Bob Gifford the deputy dean, Bob Gifford the teacher, Bob Gifford the husband and father, and Bob Gifford the teammate were on display the night of Oct. 31 when hundreds of people turned out to say farewell to Bob Gifford the friend. At a buffet dinner in Harkness Lounge, students, alumni, faculty and family laughed over remembrances of Gifford's years at Yale, which started 33 years ago when he arrived to complete his residency. Former Dean Leon E. Rosenberg, M.D., recounted how Gifford pushed the school's educational agenda and how he, Gifford and others became the first faculty members to participate in the Second-Year Show. Current student and hockey teammate Michael Fehm joked about Gifford's transfer of aggressive hockey moves from the ice to the bedside. Gifford's son Bruce told how his father dissuaded him and his three siblings from smoking at an early age—by letting them try it. Dean David Kessler amused the crowd with anecdotes about Gifford's time at Yale. "Where did he get these stories?" Gifford wondered aloud. Although he no longer has an administrative post at the medical school, Gifford remains a fixture on campus, frequently sighted at lunch with students or at faculty functions.

Bob and Karlee Gifford on the night of his farewell dinner.

FACULTY NOTES



Issam Abdullah Awad, M.D., the Nixdorff-German

Professor of Neurosurgery, was named president-elect for 1999-2000 by the Congress of Neurological Surgeons (CNS) at its annual meeting in Boston. He will assume the presidency in November. Awad has been active since 1990 in CNS, which was founded in 1951 and serves approximately 4,800 members.



Sidney J. Blatt, Ph.D., chief of the psychology section of the

Department of Psychiatry, received the Distinguished Scientific Contributions

Award from the Division of Psychoanalysis of the American Psychological Association. Blatt also was appointed visiting professor at University College in London for a three-year term. There he will participate in a summer research-training program in psychoanalysis offered in collaboration with the International Psychoanalytic Association.

James P. Comer, M.D., M.P.H., HS '66, Maurice Falk Professor in the Child Study Center and of psychiatry and one of the nation's leading experts on children, is serving on a national panel exploring the performance of minority students in schools. In a report issued in October, the College Board's National Task Force on Minority High

Achievement found that African Americans, Hispanics and Native Americans lag behind non-Hispanic whites and Asians. The report recommends that schools share information on programs that boost minority achievement. Edmund W. Gordon, Ph.D., professor emeritus of psychology, is one of the co-chairs of the 31-member task force.

John A. Eleftheriades, M.D. '76, HS '83, professor and chief of the section of cardiothoracic surgery, delivered an invited address on "High Risk Myocardial Revascularization" in October at the American College of Surgeons' annual meeting in San Francisco.

Rosemarie L. Fisher, M.D., professor of medicine and director of graduate medical

education for the School of Medicine and Yale-New Haven Hospital, has been named co-chair of the Advisory Council for the Connecticut Office of Health Care Access. The council will report annually to the Public Health Committee of the General Assembly on graduate medical education, including its financial implications for Connecticut's hospitals and its effect on access to health care and on the sufficiency of the health care provider workforce.



Roberta L. Hines, M.D., HS '77, chair of the Department

of Anesthesiology, has been elected president of the Society of Academic

Anesthesiology Chairs (SAAC). The society represents all academic anesthesiology departments in the United States and Puerto Rico. Hines will be responsible for providing leadership for both the SAAC and its component councils for two years.

Susan Hockfield, Ph.D., dean of the Yale Graduate School and professor of neurobiology, was elected a member-at-large of the Section Committee for the American Association for the Advancement of Science's (AAAS) Section of Neuroscience for a four-year term. Hockfield has been a member of the AAAS for more than 20 years. Members-at-large also serve on the committee steering group that acts on policy matters and selects nominees for fellows of the AAAS.

Jeannette R. Ickovics, Ph.D., associate professor of epidemiology and psychology, will receive the 2000 Early Career Award for Distinguished Contributions to Psychology in the Public Interest from the American Psychological Association (APA). The award will be presented in August at the 2000 APA Convention in Washington, where she will give an address entitled "Women and AIDS: Private Lives, Public Challenges."

Bruce L. McClennan, M.D., professor and chair of the Department of Diagnostic Radiology, collaborated with Walt Disney World to create an interactive exhibit on radiology that opened in October at Epcot Center in Orlando, Fla. "Radiology: Medicine's New Vision," which McClennan and colleagues from the Radiologic

Society of North America (RSNA) helped design, showcases the role of radiologists in medicine and helps explain the many new uses of radiology for both treatment and therapy. The exhibit features an arcade with several video games, including "Cell Smash," in which a guest can blast a cancer cell, and "Brain Game," which offers a virtual ride through the brain as its parts are identified. Another display allows guests a realistic try at performing an angioplasty. "I crashed the computer on my first try," said McClennan. RSNA, the largest professional radiology society in the world, made initial contact with Disney to conceive the exhibit and invested \$3 million in the project.

James R. Merikangas, M.D., lecturer in psychiatry, spoke in September at the Neurosciences and Psychiatry Congress of History in Zurich. Merikangas gave the James Joyce Lecture on "The Mental Illness of Lucia Joyce" and the Adolf Meyer Lecture on "Crossing and Recrossing the Boundary of Neurology and Psychiatry in the USA."



Robert S. Sherwin, M.D., the C.N.H. Long Professor of

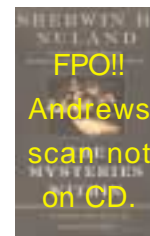
Medicine and endocrinology and director of the Diabetes Endocrinology Research Center, was named president-elect of the National Board of Directors of the American Diabetes Association at its annual meeting in San Diego. Sherwin will assume the presidency in July for a term of one year.

Albert J. Solnit, M.D., Sterling Professor Emeritus in the Child Study Center, Psychiatry and Pediatrics, was honored with a First for Kids Award in December by the Connecticut Voices for Children. Awards were presented at the New Haven Lawn Club on World AIDS Day and recognized efforts to help Connecticut children affected by the deadly virus. Solnit was recognized with a fellowship fund established in his name. Connecticut Voices for Children also established a merit award bearing his name, which was presented to state Rep. John Thompson, D-Manchester. Solnit is the commissioner of the Connecticut Department of Mental Health and was director of the Yale Child Study Center from 1966 to 1986.

Richard S. Stahl, M.D., HS '81, clinical professor of surgery (plastic surgery), has been appointed associate chief of staff of Yale-New Haven Hospital (YNHH). Stahl joined the faculty at the School of Medicine in 1983 as an assistant professor. He also serves as associate chief of surgery at YNHH.

Eiji Yanagisawa, M.D., HS '59, clinical professor of surgery and otolaryngology, received a Presidential Citation of the American Academy of Otolaryngology and Head and Neck Surgery in September at its annual meeting in New Orleans. The citation is in recognition of his efforts in the documentation of pathology and procedures, and for his talents as a teacher. Yanagisawa also was the guest of honor at the Eastern Section meeting of the Triological Society in January 1999 in Providence, R.I.

New Books



The American Disease: Origins of Narcotic Control, 3rd ed., by David F. Musto, M.D., HS '67, professor in the Child Study Center and professor of history of medicine and psychiatry, Oxford University Press (N.Y.), 1999.

Earthdance, by Lynn W. Reiser, M.D. '70, clinical professor of psychiatry, Greenwillow Books (N.Y.), 1999.

From Diapers to Dating: A Parent's Guide to Raising Sexually Healthy Children, by Debra W. Haffner, M.P.H. '79, Newmarket Press (N.Y.), 1999.

The Mysteries Within: A Surgeon Reflects on Medical Myths, by Sherwin B. Nuland, M.D. '55, HS '61, clinical professor of surgery, Simon and Schuster (N.Y.), 2000.

Our Labeled Children: What Every Parent and Teacher Needs to Know About Learning Disabilities, by Robert J. Sternberg, Ph.D., IBM Professor of Psychology and Education, and Elena L. Grigorenko, Ph.D., research scientist in psychology, Perseus Books (N.Y.), 1999.

NOTICES OF NEW BOOKS BY ALUMNI AND FACULTY MAY BE SENT TO CHERYL VIOLANTE, YALE MEDICINE PUBLICATIONS, P.O. BOX 7612, NEW HAVEN, CT 06519-0612.

STUDENT NEWS



JOHN CURTIS; (3)



Gone!

Student auction raises \$26,000 for New Haven service organizations.

An electric scooter, a week in a London townhouse and a squash game with the director of admissions were among the items that raised more than \$26,000 in the seventh annual Hunger and Homelessness Auction on Nov. 19.

Dean David A. Kessler, M.D., one of the event's auctioneers, set the tone for the levity to follow when he addressed a spirited crowd from the stage. "There are four of us," he said, resplendent in black tie and tails, "and we get graded by how much we raise."

As in past years, the auction is as much a fund-raising event as a chance to have fun. Kessler ruthlessly cajoled bidders into upping their own bids. When Special Advisor to the Dean Lawrence S. Cohen, M.D., HS '65, bid \$250 for a plane ride over New Haven, Kessler asked him for more money. "I can't bid against myself," Cohen protested. "Yes, you can," the dean replied.

Joining Kessler as auctioneers were Admissions Director Richard A. Silverman, Associate Dean for Student Affairs Nancy R. Angoff, M.P.H. '81, M.D. '90, HS '93, and Deputy Dean for Education Robert H. Gifford, M.D., HS '67. Gifford entertained the crowd by donning a leather helmet and mounting the electric scooter for a ride to the foot of the stage. "You'll do anything for a laugh," scolded Margaret J. Bia, M.D., professor of medicine. Kessler bid \$1,200 for roles in the Class of 2002's second-year show for himself, Angoff and Assistant Dean for Administration Ruth J. Katz, J.D., M.P.H.

Second-year student Nduka Amankulor and first-year Susan Rushing, both accomplished opera singers, performed a duet from *Don Giovanni*. The Ultrasounds, an a cappella group comprised of students of medicine, nursing, public health and the Physician Associate Program, sang Van Morrison's "Moondance." Amankulor, second-year medical student Hung Nguyen and public health student Betsy Luo organized the auction.

Proceeds will benefit Columbus House, Youth Continuum, New Haven Cares, Rachel's Table and St. Luke's Services.

The student-run Hunger and Homeless Auction has become a yearly outlet for talent, exuberance and creativity.

1 Medical students Susan Rushing and Nduka Amankulor performed a duet from *Don Giovanni*. 2 Dean David Kessler auctioned a puppet show, to be performed by Bob Gifford. 3 Second-year students Nikki Pinkerton and Mary-Ann Etiebet sat back and enjoyed the show.

Getting things done in the field

Downs fellows return from their travels with an appreciation for the practical.

Foreign fieldwork sometimes requires seat-of-the-pants skills beyond drawing blood or crafting a health survey. During assignments that took them to Africa, Asia, Latin America and Russia last summer, students learned, as medical student Vivek Murthy put it, “who you need to know to get things done.” Good communication is also important, Murthy found when he asked villagers in India to participate in a study of iron-deficiency anemia among teenagers. As part of the study he requested matchbook-sized stool samples. “That information got lost,” Murthy said. “We went to one school and found students bringing in bags of stool. In another, we had students bringing in stools that you sit on.”

Murthy and 14 other students traveled under the auspices of the Wilbur Downs International Health Travel Fellowship Program. They presented findings from their investigations in October at the annual fall symposium and poster session of the Committee on International Health.

For 31 years, students in medicine, nursing, public health and the Physician Associate Program have received Downs grants for studies abroad. Topics presented in October included the use of female condoms in Kenya, the involvement of Egyptian men in reproductive health decisions, interventions in South Africa to reduce vertical transmission of HIV, women’s health in Mexico City and the impact of sanitary sewage disposal on children’s malnutrition in Kosovo.

Erik Hett learned to improvise in Kenya when a sudden electrical failure sent him scurrying in search of a generator to power his centrifuge. Without power, hours of work dissecting and preparing tsetse flies for analysis would be lost. Hett, a student in public health, hoped to determine whether the *Wolbachia* bacterium could kill the tsetse fly before the fly grew old enough to transmit the parasite that causes sleeping sickness. (His faculty advisor was Scott O’Neill. See related story, page 16.) Hett and co-worker Rhoel Dinglasan, a doctoral candidate in public health and previous Downs fellow, finally found a working electrical generator in a local hair salon and, despite language barriers and quizzical looks from patrons, secured permission to plug in their centrifuge.

The two trapped their flies in the bush, where they learned another lesson not taught in school. “The flies tried to follow the buffaloes,” Hett said, “so we had to make sure the traps were close to the buffaloes.”

Murthy, who enjoyed collaborating with health workers in India, including doctors and nurses, said it was important to weigh his priorities and needs against those of the local population. “It is always a struggle to find a balance between them,” he said. “Listening to the local people was a critical part to making this successful.”



Public health student Anusha Sinha describes her research on “Antibiotic Prescribing Patterns in Nagpur,” which was supported by the Coca Cola World Fund.

Healing after torture

A Yale student looks at the link between scar and symptom.

Shadowing clinicians at Bellevue Hospital in New York City last summer, medical student George Lui heard questions most doctors never have to ask their patients.

“Who tortured you?”

“Where and when did it happen?”

“Can you tell me more about it?”

Lui worked in the Bellevue/NYU Program for Survivors of Torture, which offers multidisciplinary services to people who have experienced physical or psychological torture. The program provides long-term treatment to patients and their families, combining medical, psychiatric, psychological and social services provided by a variety of health professionals. Working under program director Allen S. Keller, M.D., Lui’s task was to review charts of the approximately 250 active patients in the program and look for correlations between specific forms of torture and individual symptoms. Such information could help clinicians develop more effective strategies for working with victims of torture.

His apparently straightforward review took some twists and turns, Lui said. Cultural and religious habits and beliefs often dictated how people responded to torture. Tibetan torture survivors, he noted, do not often meet formal criteria developed in the west for a diagnosis of post-traumatic stress disorder because they don’t avoid thoughts or activities associated with the trauma. Avoidance, however, is one of the three pillars of PTSD diagnosis.

Clinicians often were unable to distinguish between symptoms that resulted from torture and psychosomatic symptoms resulting from psychological distress. Lui cited the case of a 57-year-old woman from Sierra Leone. Trapped in her village during a battle, she watched as rebels burned her house and murdered her relatives. After receiving death threats, she came to the United States. “Once this summer she came to the clinic complaining of abdominal pain,” Lui said, recalling the medical consultation he observed. “Is this a sequela of her trauma history or an unrelated medical manifestation?”

In his report, funded by the David E. Rogers Student Research Fellowship from the New York Academy of Medicine and the Yale School of Medicine Summer Fellowship, Lui listed forms of torture applied, countries of origin of the survivors and how the trauma was manifested. Beatings were the most common form of torture, followed by deprivation of food and water. Imprisonment was the most common psychological torture, followed by murder of relatives. Most survivors in the program, 39 percent, were from Africa, followed by Tibet, 34 percent. And most, like the woman from Sierra Leone, suffered from PTSD.

“She started to talk about her trauma history and she broke out in tears,” Lui said. “It’s really important to listen to these stories because that could greatly influence how you treat torture survivors.”



JOHN CURTIS

New alumni affairs director is named

Sharon R. McManus, a seasoned professional with experience in both alumni affairs and development at Yale for the past 13 years, has been named director of alumni affairs at the School of Medicine.

McManus is familiar to many Yale medical graduates who have attended alumni events or been assisted by the Office of Alumni Affairs in recent years. She came to the University in 1987 to join the staff of the Yale Alumni Fund, serving the graduate and professional schools; two years later, she moved to the medical school's Office of Development. McManus joined the Office of Alumni Affairs in 1997 and was promoted from administrative associate to assistant director in the spring of 1999.

In announcing the appointment, Associate Dean Jane E. Reynolds praised McManus as "a true profes-

sional whose efficient, thoughtful and energetic presence will advance not only the goals of the alumni affairs office, but those of the entire enterprise." Along with long-time staff member Patricia DiNatale, McManus will work closely with the Association of Yale Alumni in Medicine and the Medical Alumni Fund Board. A search is under way to fill McManus' previous position.

"I'm honored to be working with the alumni of the medical school. The devotion they show to their alma mater is inspiring," said McManus, who succeeds William K. Jenkins, now at Drew University.

"Party and I both want to see the alumni activities that we have in place continue, and we want to see what can be enhanced."

New projects under way include a Web-based program to enlist alumni as mentors for current students, especially during the residency application process. In addition, several events bringing alumni and students together are planned for the remainder of the year. Alumni Reunion Weekend will be held June 2 and 3 (See page 48).



Alumni turn out for 'The Game'

Among the crowd of thousands at the Yale Bowl who watched the football team squeak by Harvard in the annual November match known simply as "The Game" were 500 alumni of medicine, public health and the house staff. Over a lunch of barbecued chicken, hamburgers, veggie burgers and New England clam chowder, alumni renewed old ties with each other before moving into the stands for the game. A last-minute touchdown clinched Yale's 24-21 victory.

MELANIE STENDEL (3)

CORRECTION

Three photographs were transposed on page 43 of the Fall 1999 | Winter 2000 issue of *Yale Medicine*. The correct identifications appear at right.



Valerie E. Stone, M.D., '84
Representative to the AYA



Susan J. Baserga,
M.D. '88, Ph.D. '88
Member, Executive
Committee



Christine A. Walsh,
M.D. '73
Member, Executive
Committee

30s



Roy C. Robison, M.D. '36, B.A. '32, writes to say that

he is living in Tucson, Ariz., after retiring in 1979 from his ob/gyn practice in Connecticut. During his career, he was vice president of St. Joseph's Hospital in Stamford, Conn., from 1966 to 1969.

50s



Marie-Louise Johnson, Ph.D. '54, M.D. '56, HS '59, a Kingston,

N.Y., dermatologist, is the first woman to be elected president in the 123-year history of the American Dermatological Association. The announcement was made during a conference in Vienna in July. She is serving as president-elect until July 2000, when her one-year presidency begins. Since graduation from Yale School of Medicine, her professional career has been a series of first achievements by a woman in medicine. Those honors include being the first female dermatologist elected to the National Academy of Sciences, Institute of Medicine, and the first woman presidential candidate of the American Academy of Dermatology (AAD), both in 1981. In 1995 she was the first woman recognized by the AAD as a Master in Dermatology, and in 1997 was the first woman to receive the Finnerud Award of the Dermatology Foundation for excellence in clinical practice,

teaching and research. Johnson, also active in the Association of Yale Alumni in Medicine since 1985, was its president from 1993 to 1995 and received the Distinguished Alumni Service Award in 1996.

Kristaps J. Keggi, M.D. '59, HS '64, received the Fifth Class Order of the Estonian Red Cross in a ceremony at the Estonian Embassy in Washington. The award, presented for outstanding medical service to that nation, is one of Estonia's highest medical honors. Keggi also was recognized as an outstanding teacher by the residents in the Department of Orthopaedics and Rehabilitation at Yale for his continued contributions and dedication to the resident education program.



James A. O'Neill Jr., M.D. '59, chair of the section of

surgical sciences and the John Clinton Foshee Distinguished Professor of Surgery at Vanderbilt University in Nashville, was installed as president of the Southeastern Surgical Congress in February at the annual meeting in Lake Buena Vista, Fla. The organization, founded in 1930, meets the needs of general surgeons for continuing their education beyond medical school and represents over 3,000 general surgeons in the Southeast, Puerto Rico and the District of Columbia.

60s



Philip D. Manfredi, M.D. '65, writes to say that he and

his wife, Joann, had a wonderful time and met some great people on the Association of Yale Alumni's Alumni College Abroad Program. Their trip was called "Autumn in Burgundy and Provence."



Clarence T. Sasaki, M.D. '66, HS '73, the Charles W. Ohse

Professor of Surgery and chief of Yale's section of otolaryngology, was honored by the American Laryngologic Association with the Casselberry Award for leading research in the area of basic laryngeal function. His research focuses on motor innervation of the cricopharyngeus muscle, the muscle that controls the upper esophageal sphincter and is involved in breathing and swallowing.

70s



John D. Bullock, M.D., HS '74, chair of the Department

of Ophthalmology and professor of physiology and biophysics at Wright State University's School of Medicine in Dayton, Ohio, received the university's 1999 Brage Golding Distinguished Professor of Research Award. His research uses mathematics

and physics to explain how improper administration of anesthesia can lead to eye injury.

80s

Patrice K. Rehm, M.D. '81, HS '87, assistant professor of radiology at Georgetown University Hospital, was named a fellow of the American College of Radiology for outstanding contributions to this specialty. The award was bestowed in September during the annual meeting held in Washington.

90s



Erika H. Newton, M.D. '90, sent us a postcard from Panama City

to say that she is currently on extended leave from a staff position in the Emergency Department at Mount Auburn Hospital and a teaching appointment at Harvard Medical School. She is circumnavigating the globe in a 35-foot sailboat with her husband. They recently transited the Panama Canal and were due to cross the Pacific this spring.



Redentor L. Galang, M.D., a postdoctoral fellow in geriatric psy-

chiatry at Yale in 1999, was appointed assistant professor of psychiatry at Southern Illinois University School of Medicine in September.

In memoriam

Miguel R. Alonso, M.D.

Mae Rhend Gailani, M.D.

William F. Heidenreich, M.D.

J. Peter Murphy, M.D.

Paul B. Sigler, M.D., PH.D.

Maurice Van Lonkhuyzen, M.D.

Brig. Gen. Thomas J. Whelan Jr., M.D.

Miguel R. Alonso, M.D. '63, of Tampa, Fla., died Aug. 30 of renal cell carcinoma. He was 61.

A native of San Juan, Puerto Rico, Alonso followed in his father's footsteps and studied otolaryngology. After graduating from the School of Medicine, he served his internship at St. Vincent's Hospital and Medical Center in New York. From 1964 to 1969 he was a resident at the Johns Hopkins Hospital. As an Air Force major treating the wounded in Vietnam, he received decorations from three governments—Korea, the Republic of Vietnam and the United States. Alonso served at the University of Texas Medical Branch as an assistant professor until 1972.

In 1975 Alonso moved his family to Tampa, where he started his practice and began teaching at the University of South Florida. He was in private practice and an associate professor in the Department of Otolaryngology at the university until his death. During his career he also served as president of the Hillsborough County Medical Association.

Mae Rhend Gailani, M.D., of Guilford, Conn., died Nov. 24. She was 39.

Gailani came to Yale in 1990 as a postdoctoral fellow in pediatrics. In 1993 she joined the faculty as an associate research scientist in pediatrics and became an assistant professor of pediatrics and neonatology in 1996. In addition to her expertise in neonatal medicine, Gailani was a significant contributor to research on inherited cancers. To recognize her devotion to her patients and her outstanding research accomplishments, the Department of Pediatrics named the recently established Young Investigator Award in her memory.

Gailani was the wife of Steven E. Pfau, M.D., assistant professor of medicine and cardiology at Yale.

William F. Heidenreich, M.D. '55, died Sept. 30 at his home in Marquette, Iowa.

Born in Pittsburgh, Heidenreich attended Yale University, receiving his bachelor's degree in 1951 and his medical degree in 1955. He did his residency at the University of Chicago from 1956 to 1959. He served for two years with the Army in Panama, before returning to Connecticut to work at the Veterans Affairs Medical Center in West Haven.


Heidenreich then moved his family to Dubuque, Iowa, where he practiced radiology

and nuclear medicine at Mercy, Finley and the former Xavier hospitals. In 1978 they moved to Utah, where he was on the staff at the Cedar City Hospital. In 1981 they returned to Iowa, where he served on the staff in the community hospitals of Waukon, Elkader, Cresco, West Union and New Hampton. He retired from medical practice in 1987.

J. Peter Murphy, M.D. '39, died Jan. 13, 1999, in Bethesda, Md., after a prolonged illness. He was 82.

Born in 1916, in Aitkin, Minn., Murphy graduated from St. Thomas College in 1935. He graduated magna cum laude from the Yale School of Medicine in 1939, receiving the Campbell Medal for the highest-ranking medical student. His post-graduate training, which began at the New Haven Hospital, included pathology and neuropathology and ultimately led to a career in neurosurgery.

Murphy was an associate professor of neurological surgery at The George Washington University for many years and had a private practice at Suburban Hospital in Bethesda, Md. He also served at other hospitals in the Washington area. He authored many medical articles and one book, *Cerebrovascular Disease*.



According to his son, Michael, Murphy was devoted to Yale and sent his three sons there for their undergraduate education. All three followed him into medicine. A major highlight of his life was attending his 55th medical school reunion, where he was able to renew acquaintances from his time in New Haven.

Paul B. Sigler, M.D., Ph.D., died Jan. 11 after suffering a heart attack while walking to his laboratory at Yale. He was 65.

Born in Richmond, Va., Sigler received his medical degree from Columbia University in 1959 and a doctorate in biochemistry from Cambridge University, England, in 1968. He served his internship and residency at Columbia-Presbyterian Medical Center.

In the early 1960s, Sigler did research at the National Institutes of Health to unravel the secrets of enzyme function. He then joined the staff of the Medical Research Council Laboratory in Cambridge, England, where in 1967 the research group he was working with succeeded in determining the atomic structure of the second enzyme to be solved.

Later in 1967 Sigler joined the faculty of the University

of Chicago, attaining the rank of professor of biochemistry and molecular biology. In 1989 he joined the Yale faculty and the Howard Hughes Medical Institute, serving as a professor of molecular biophysics and biochemistry until his death. The National Academy of Sciences selected Sigler, in 1992, as an advisor to the federal government.

Among his technical achievements was the structure determination of a large assembly of protein whose function was to form a machine that assures the correct folding of other newly synthesized proteins into the proper three-dimensional structure. This macromolecular machine is among the largest structures solved and provided unprecedented mechanistic insights into a catalyzed process unknown until recently.

As one of the world's leading structural biologists, Sigler's primary research interest was the chemistry of cellular regulation, focusing on the mechanisms by which gene expression is controlled, how transmembrane signaling is accomplished and the way that an enormous protein machine called a chaperonin assists in the correct folding of the proteins. His goal in all of these studies was to provide the basis of fundamental biological processes in terms of stereochemistry.

Maurice Van Lonkhuyzen, M.D. '52, HS '56, of Falmouth, Maine, died Nov. 26 at a hospital in Portland. He was 77.

Born in Chicago, Van Lonkhuyzen grew up in the Netherlands. In 1941 he returned to the United States and served in the Army during World War II. He graduated from Michigan State University and in 1952 received his medical degree from Yale. Van Lonkhuyzen served his internship at Maine General Hospital and was an ophthalmology resident at Grace-New Haven Hospital.

In 1956 he opened his private practice in Portland and introduced corneal transplant surgery in that region. He retired in 1995. During his career Van Lonkhuyzen served as chief of the Department of Ophthalmology at Maine Medical Center, staff surgeon at Mercy Hospital and president of the Cumberland County Medical Society. He also served as president of the medical staff at Pineland Center and president of the board of directors of the Maine Institute for the Blind.

Brig. Gen. Thomas J. Whelan Jr., M.D. '46, of Honolulu, died on Sept. 10 after suffering complications and a stroke following hip replacement surgery. He was 78.

A native of Lynn, Mass., Whelan received his bachelor's degree in 1943 and his medical degree in 1946, both cum laude from Yale. He was captain of the Yale baseball team. Following his internship and residency at Strong Memorial Hospital in Rochester, N.Y., he began his career as a military surgeon, which included service in the Korean War.

Whelan was chief of surgery at Tripler Army Medical Center in Hawaii and later held the same post at Walter Reed Army Hospital. He was also a special assistant to the Army Surgeon General, responsible for positioning military physicians worldwide. He retired from the Army in 1973 and became affiliated with the University of Hawaii, where he served as chairman of surgery and director of internship/residency programs until his retirement in 1990.

Yale University School of Medicine

Alumni Reunion Weekend

Program Highlights

Friday and Saturday, June 2–3, 2000

Friday, June 2

minority alumni luncheon
alumni fund class agents &
reunion gift chairs luncheon
ayam executive committee
luncheon meeting
class reunion programs
Class of 1960 – 40th Reunion
Class of 1995 – 5th Reunion

The Many Faces of Medicine

the importance of affirmative
action to the health care of
our nation
keynote speaker
Augustus A. White III, M.D., Ph.D.

the student perspective:
life at Yale today

moderator Nancy R. Ango, M.D. '90
minority student panel
Paola Uranga '03
Kevin Johnson '02
Rashida N'Gouamba '02
Jose Miranda '01

the alumni/faculty perspective:
life after Yale

moderator Forrester A. Lee, M.D. '79
panelists
Kamau B. Kokayi, M.D. '82
Yvedt L. Matory, M.D. '81
Donald E. Moore, M.D., M.P.H. '81
O'Dell M. Owens, M.D. '76

Yale Surgical Society presentation
and reception
dean's reception
New England Clambake

Saturday, June 3

breakfast
minority reunion
steering committee breakfast

Mapping the Future:

The Human Genome Project,
Yale Perspectives

Panel Discussion

moderator Carolyn W. Slayman, Ph.D.
panelists
Richard Lifton, M.D., Ph.D.
Margretta R. Seashore, M.D.
David C. Ward, Ph.D.

annual meeting of the association
of Yale alumni in medicine

sherry/buffet luncheon

class reunion program
Class of 1955 – 45th Reunion

guided tours

Yale Center for British Art
Historic Sections of New Haven

planned giving open house

For information contact:

Sharon R. McManus, Director,
Office of Alumni Affairs
Yale University School of Medicine
P.O. Box 7613, New Haven, CT 06519
(203) 785-4674
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Association of Yale Alumni
in Public Health
Spring Workshop and Annual Meeting

The Future of Public Health in the 21st Century

*Water's Edge Resort and
Conference Center, Westbrook, ct*

Friday, June 2

Workshop: Reinventing Health Care

moderator Henry Dove, ph.d.

panelists

Karen A. Coughlin, m.a., b.s.n.
William L. Kissick, m.d. '57, dr.p.h. '61
Timothy B. Norbeck, dms
Bruce I. Taylor, clu, m.b.a.
Gail Wilensky, ph.d.

Alumni Reunion

awards luncheon

keynote address:

Gail Wilensky, ph.d.

The Future of Public Health in the 21st Century

approaching the limits
of global health and wellbeing

alumni panel

alumni poster session

dean's reception

new england clambake

first annual john thompson

health management dinner

Registration for each of these events is separate.
Please contact Dawn Carroll, Office of
Community and Alumni Affairs, Yale School of
Public Health, P.O. Box 208034, New Haven, ct
06520, by phone (203) 785-6245, or e-mail
dawn.carroll@yale.edu

Parking will be available all day at Water's Edge
and after 5 pm at College Plaza and the Graduate
Club. If you need transportation from eph to
Water's Edge you must register with Dawn Carroll
by May 15, 2000.



Yale University School of Nursing
Alumnae/i Association
43rd Annual Alumnae/i College Weekend

ysn in y2k: High Tech, High Touch

Friday, June 2

minimizing the human
cost of advancement

the year in review

lunch

plenary sessions

class agents meeting

social hour and banquet

Saturday, June 3

continental breakfast

yusnaa annual meeting

new world of diabetes:

advances in care

lunch

For further information, contact Barbara F. Reif,
Director of Student and Alumnae/i Affairs,
Yale University School of Nursing,
100 Church Street South, P.O. Box 9740,
New Haven, CT 06536-0740
Tel. (203) 785-2389

Continuing Medical Education at Yale

June 10 (Saturday)

"Primary Care Update 2000:
Snoring & Sleep Apnea"

Course Directors:

Douglas Ross, M.D.

Vahid Mohsenin, M.D.

Clarence T. Sasaki, M.D.

*Foxwoods Resort and
Conference Center, Ledyard, CT*

September 8 (Friday)

"Fourth Annual Yale
Glaucoma Symposium"

Course Director:

M. Bruce Shields, M.D.

Water's Edge, Old Saybrook, CT

September 9 (Saturday)

"Pulmonary Conference"

Course Director:

Carolyn M. D'Ambrosio, M.D.

Foxwoods Resort and

Conference Center, Ledyard, CT

September 14-16 (Thurs-Sat)

"Technically Challenging
Procedures in Adult
Cardiac Surgery"

Course Director:

John A. Elefteriades, M.D.

Foxwoods Resort and

Conference Center, Ledyard, CT

October 13 (Friday)

"The Moshe Lahav Lecture in
Ophthalmic Pathology"

Course Director:

M. Bruce Shields, M.D.

Harkness Auditorium

October 19 (Thursday)

"Third Annual Frisbee
Stem Cell Symposium"

Course Director:

Edward Snyder, M.D.

Omni Hotel, New Haven, CT

October 21 (Saturday)

"EEG in Clinical Psychiatry"

Course Director:

Nash Boutros, M.D.

Jane Ellen Hope Building,

Room 110

For information, contact the
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Continuing Medical Education,
Yale University
School of Medicine
333 Cedar Street
New Haven, CT 06520
Tel: (203) 785-4578

