A week at the beach or a week at the bench? Science won out for two dozen students who spent part of their summer break in the lab in Maine, but the scenery wasn’t bad either. Page 18.

Illustration by Calef Brown

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

Explore the following topics in greater depth by visiting our website and selecting extras:
– The Historical Library’s online exhibit about the School of Medicine’s early 20th-century history
– The Mt. Desert Island Marine Biological Laboratory
– The International Health Program
– Additional photos from Alumni Reunion Weekend

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

SHARKS, SALT (AND A TASTE OF LOBSTER)
An intensive week at the bench in Maine introduces students to modern lab strategies and techniques, ancient DNA and a clambake to write home about.
by John Curtis

A WORLD OF DIFFERENCE
Yale’s International Health Program sends young doctors around the globe to provide needed care—and learn the basics of a simpler medicine.
by Cathy Shufro

AN EPIDEMIC IN THE MAKING
Type 2 diabetes poses alarming health risks as obesity rates soar and exercise is crowded from modern life. Yale investigators are seeking better ways to prevent and treat the disease and to understand the science of fat.
by Randi Hutter Epstein

FACULTY
STUDENTS
ALUMNI
IN MEMORIAM
ARCHIVES
COMMUNICATION STILL DOESN’T COME EASY

I read with interest your article entitled “A Dramatic Turn” [Spring 2001] regarding the physician-patient relationship. I suspect my experience during my tenure at Yale in the early 1980s was fairly typical. I certainly received the message that truly caring about a patient as an individual was very important, but I did not receive any training regarding how to make that “caring” experience happen on any consistent basis.

This article tells me that Yale still cares very much about the patient. But I was disappointed to note its emphasis on how to make the physician-patient relationship happen within the short appointment reality of primary care today.

I am now one of the chiefs of ophthalmology with Kaiser and The Permanente Medical Group (HPM) in California. I have just been recruited to be the “local communication consultant” in our facility. Communication consultants like myself are given training on the essential elements of an effective patient-provider interaction. These evidence-based elements have been dubbed the “Four Habits of the Highly Effective Clinician.” They form the backbone of an eight-hour curriculum which teaches the participants four key skills that allow the physician to make a satisfying connection with the patient—often within a 15-minute interaction.

Awareness-building presentations like those of Dr. South’s are highly valuable. I think the next step might be offering our physicians in training a program similar to HPM’s, one that teaches specific and attainable techniques to improve communication.

Eilam Kolker, M.D.
By Patrick Sullivan

TAKING THE PULSE OF HEALTH INTERACTIONS

In the Spring 2001 issue, the article “A Dramatic Turn” provoked a thought-provoking look at the physician-patient relationship.

We want to call your attention to another Yale-based initiative that examines the physician-patient relationship. The Program for the Study of Health Care Relationships, funded by the Patrick and Catherine Wal- don Donaghue Medical Research Foundation, is a collaborative project between Yale University and the University of Connecticut. The program’s mission is to bring together the relational aspects of care to the forefront of the ongoing discussion about health care in Connecticut and the nation. It seeks to enable patients, health care professionals, providers, health policymakers and other interested individuals to engage in successful partnerships, with the shared goal of improving patient outcomes, especially in the context of adherence to therapeutic regimens. A multidisciplinary team has been working for a year to study the relational aspects of care and their effects on adherence.

The interdisciplinary program provides a forum for a range of issues, including health education; the role of the Internet and technology; the influence of organizations, insurance and policy; and the relationships among professions, as well as with patients. The group consists of physicians, nurses, social workers, consumers, academics and others, and has a website: info.med.yale.edu/ nursin/hist/!

Please join us, Ph.D., P.G.S., director, Program for the Study of Health Care Relationships, associate professor, Yale School of Nursing.

THANK YOU FOR AN OUTSTANDING MAGAZINE

May I take this opportunity to comm- mend you on the excellent quality and caliber of Yale Medicine. It is outstanding, informative, insightful and pleasurable to read. Thank you for your superior effort.

Lash F. Fremon, M.D.
Baltimore, MD

HOW TO REACH US

Yale Medicine welcomes news and commentary. Please send letters to the editor and news items to Yale Medicine, P.O. Box 1622, New Haven, CT 06509-0162, or via electronic mail to ymm@yale.edu, and include a daytime telephone number. Submissions may be edited for length, style and content.

FROM THE EDITOR

Walking a fine line

Every so often someone will offer an idea for an article or a comment about a piece they read in “the journal,” meaning Yale Medicine. Along with my thanks, I usually note that Yale Medicine is more journalism than jour- nal, a magazine rather than a medical tome. This is an important distinc- tion in academia, where the peer-reviewed scrutiny and serious aims of scientific publishing reflect one set of core values.

We’re a slightly different animal. Our primary goal is to keep alumni in touch with each other and informed about the work and scholar- ship that goes on here. Our objective is to be intriguing to a wide audience and still relevant to each of our readers, whose interests run the gamut from structural biology to the history of medicine. As cartoonist Sidney Harris observes below, what one subspecialist finds hopelessly gen- eral may be incomprehensible to another learned person. It is our intent to bridge that gap in a way that readers will find engaging.

We hope you’ll let us know how we’re doing. As this issue went to press, we received some welcome feedback from the Association of American Medical Colleges, which honored Yale Medicine with its highest level of recognition, the Award of Excellence. Also this issue, we are completing the final phase of the magazine’s redesign. I appreciate the suggestions we’ve received along the way and hope you like the result.

Michael Fitzsousa
mfitz@yale.edu

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**THE STRONDEST KIND OF LETDOWN**

On September’s day of terror, Yale geared up to treat survivors who never came.

On September 11, a day of death and panic elsewhere, there was an odd sort of quiet in New Haven. In the medical school’s clinics and classrooms, the day’s routine activities fell by the wayside, overwhelmed by the horror of what was happening in New York, Virginia and Pennsylvania. The medical center geared up for an onslaught of trauma cases that never materialized. For 24 hours, Yale-New Haven Hospital was an disaster alert for survivors who might have been pulled from the wreckage of the collapsed World Trade Center only 90 miles away. But, said a hospital spokeswoman, “It was the strangest kind of letdown.”

Medical school faculty and alumni who provided aid in Lower Manhattan experienced a similar disappointment. Emergency physician Scott Weir, m.d., a veteran of search and rescue efforts including the 1998 bombing of the U.S. embassy in Nairobi, had never seen anything like the devastation at the World Trade Center. During a week on the scene he treated no survivors, only rescuers with minor injuries. Kenneth C. Rondello, m.p.h. ’94, m.d., spent four days at the blast site and Chelsea Piers, where an ice rink became a morgue and the set of television’s “Spin City” a trauma center. “No news footage you’ve seen or descriptions you’ve heard can truly do it justice,” he said. “The air was permeated with the nauseating, acrid smell of burning jet fuel. Everything was covered in inches of gray ash, as if a volcano had erupted.”

Life went on at Yale but the tragedy haunted everything that followed. No gathering could begin without some acknowledgement of “the events of September 11.” The day of the attacks, classes were canceled for first- and second-year medical students, some of whom traveled to New York to volunteer in the Office of the Chief Medical Examiner. That first night, hundreds of students and faculty members carried candles down College Street to a vigil at Cross Campus.

In the days that followed, the University responded with drives for blood and donations, along with lectures and discussions on terrorism, foreign policy and Islam. Students at the School of Public Health held a teach-in. Medical and public health students visited local merchants of Middle Eastern descent to reassure them at a time when they might fear discrimination. On September 28, speakers invited by the Department of Psychiatry and the Child Study Center explored the ways in which people cope with a world turned upside down.

Among those determined to get on with their lives were Edwin Thrower, ph.d., a postdoctoral associate in the Department of Pharmacology and his fiancée, Bozena Sakowska. They decided to go ahead with their wedding September 15, even though his parents and friends in England could attend only via a conference call. The ceremony included a prayer for victims of the attacks, and ended on an upbeat note. “We had friends come from Manhattan,” Thrower said. “They said this was very much needed—a celebration of joy, love and life.”

**STEM CELL SCIENTIST URGES CONGRESS TO FUND EMBRYONIC RESEARCH**

When Diane Krause, m.d., ph.d., published findings this spring from her work on adult-derived stem cells in mice, she didn’t expect to become a player in a national political debate. “I thought it would be important for those of us in the field,” she said in July, adding “I didn’t realize it was going to get such press attention.”

Krause, an associate professor of laboratory medicine and pathology, identified adult stem cells in bone marrow that can also create new liver, lung, gastrointestinal and skin cells. Working with collaborators at Johns Hopkins and New York University, she found the first evidence that these progenitor cells are capable of creating up to 15 different mature cell types (See Findings, page 13).

Since the publication of her work in the May issue of Cell, Krause has been besieged by media inquiries from around the world. In early summer, she was asked to testify on Capitol Hill.

Her conclusions were published as the national debate over embryonic stem cell research was heating up and, to her dismay, have provided fodder to opponents of such work, which requires the destruction of human embryos. Those who oppose embryonic stem cell research for moral reasons argue that it is unnecessary because adult stem cell research shows promise. Krause insists that research done both avenues is vital.

In July she had a chance to make her point before the U.S. Senate Appropriations Subcommittee on Labor, Health and Human Services and Education, which held hearings on the federal government’s role in funding future embryonic stem cell research.

Embryonic stem cell research needs to be funded for three reasons, Krause told the subcommittee. First, these cells can be grown in vitro, unlike adult stem cells. Second, because they are the most versatile cells available, embryonic stem cells yield far more information on how they maintain that versatility than adult-derived cells. And third, she said, “No one can predict which lines of investigation will lead to effective and safe treatments for human disease.”

On August 9 President Bush outlined his plan for funding embryonic stem cell research: only existing lines of embryonic stem cells, left over from in vitro fertilization, could be used in federally funded research. Research using embryonic stem cell lines developed after August 9 would be ineligible for funding. On August 27, the National Institutes of Health released a list of 64 eligible embryonic stem cell lines. Scientists have questioned that list, noting that many cell lines are unavailable or inappropriate for a variety of reasons.

“The president’s plan is not well thought out,” Krause said. “It doesn’t give federally funded scientists the freedom to pursue scientific questions.”

On September 5, Secretary of Health and Human Services Tommy Thompson told a Senate committee that only about 24 of the 64 cell lines were ready for use in experiments. The usefulness of the remaining cell lines, he said, remains to be proven.
FROM THE AUTOPSY SUITE, A TREASURE TROVE
OF "POST-MORTEMISM"

Before photography became the standard for capturing images of important anatomical findings, pathology departments hired specially trained illustrators to create visual materials for teaching and recording medical knowledge. Among the most gifted among them was Armin Bismark Hemberger, whose career at Yale spanned six decades.

Hemberger, who lived from 1896 to 1974, is the subject of new interest and may someday be featured in a documentary film and traveling exhibit.

A student of Max Brödel, who is widely regarded as the father of American medical illustration, Hemberger worked in the tradition of Weislaw, daVinci and Düür, combining artistic skill with a remarkable level of scientific accuracy to produce brilliant images in pen and ink, pencil, gouache and watercolor. Approximately 700 of these drawings are preserved in the illustration collection of the Department of Pathology.

"Hemberger was one of the best," said Ranice W. Crosby, director emerita of the Department of Art as Applied to Medicine at Johns Hopkins, where Brödel's papers are archived.

Born in Scranton, Pa., on April 1, 1896, Hemberger graduated from the Maryland Institute of Art and Design in Baltimore. In 1917, he was recruited by Milton C. Winternitz, m.d., as a medical illustrator for the New Haven Station of the Army Chemical Warfare Service. His drawings are in two classic monographs edited by Winternitz, Collected Studies on the Pathology of War Gas Poisoning and The Pathology of Insecticide. Hemberger returned to Baltimore in 1920 for a year of study with Brödel before spending the remainder of his career at Yale. He retired in 1962.

In addition to his medical work, Hemberger painted landscapes and is represented in the collection of the Metropolitan Museum of Art in New York.

In 1987, during the construction of a new autopsy suite, faculty member Raymond Yesner, m.d., noticed two large filing cabinets that had been pushed into the old dissection room. "I was absolutely knocked over by what I saw — hundreds of Hemberger's paintings and drawings stacked one on top of the other," an e-mail to catalog the images began in earnest and stops to preserve the original works followed. Five years ago, Jon S. Morrow, ph. d., ’74, m.d., ’76, h. ’77, chair of the Department of Pathology, asked Katherine Henderson, the department's photography and graphics manager, to begin digitizing the illustrations and transferring the original works into acid-free, archival containers. Working with Deborah Dillon, m.d., ’92, a faculty member who provided annotation for many of the drawings, this task has now been largely completed.

"The drawings are living, breathing documents of a different kind of Yale," said Morrow, who collaborate with students in Brödel's paper style. "It was a different world, a different time, a different place, a different culture," said Morrow.

Hemberger's work has guided generations of medical students and physicians in training. One of them was Virginia Alvaro, m.d., who said the artist "had an incredible ability to summarize the essence of the anatomical findings of a given condition in a single illustration."
SLOT MACHINES AND THE CINGULATE CORTEX

The neurobiology of pathological gambling bears striking similarities to that of drug craving.

From the green towers of the world’s largest casino rising up from the Connecticut farmland to the smash-hit television program Who Wants to Be a Millionaire, a culture that promotes and glorifies gambling is all around us. But until recently, little has been done to investigate gambling addiction, a significant health problem that may be as prevalent as some other major psychiatric illnesses such as schizophrenia, pervasive developmental disorders, and mood states. While further study is needed, the neuroimaging study may help identify a possible intervention point for treating pathological gambling.

The Problem Gambling Clinic, a collaboration between Yale’s Department of Psychiatry and the Connecticut Mental Health Center, took advantage of the recent proliferation of brain scanning technologies to study pathological gambling. To view controlled cues that trigger the urge to gamble, patients who have viewed videotaped cues are scanned using functional magnetic resonance imaging and functional assessments. Afterward, the patients are asked to rate the cues’ ability to trigger urges to gamble.

A number of drug addiction studies have investigated the brain’s response to stimuli that trigger other drug cravings. Potenza and his colleague John vaping (it is not known why) to the study.

Problem and pathological gamblers, though, have had few treatment options available. For example, about 75 percent of callers to the Connecticut Council on Problem Gambling’s hotline reported never having received any prior help for a gambling problem. Potenza is working to change that.

The Problem Gambling Clinic, a collaboration between Yale’s Department of Psychiatry and the Connecticut Mental Health Center, is one of only four sites in the U.S. to participate in the first multicenter trial of a drug to treat compulsive gambling. Initial data from the trial evaluating the effects of naltrexone (a pain reliever) are encouraging, said Potenza. He is also using functional magnetic resonance imaging to monitor the brain activity of both gamblers and healthy subjects who have viewed videotaped cues intended to spark the urge to gamble. Only in the pathological gamblers did viewing the cues lead to lower activity in the anterior cingulate cortex, a brain region which has been repeatedly implicated in previous studies of drug craving and mood states.

While further study is needed, the neuroimaging study may help identify a possible intervention point for patients with the addiction.

MULTIPLE SCLEROSIS THE TARGET OF EXPERIMENTAL SCHWANN CELL TRANSPLANT

Physicians and researchers are hoping that cells from a nerve in a patient’s ankle will stem the degeneration of the nervous system caused by multiple sclerosis.

In July a Yale team transplanted Schwann cells from the sural nerve into a patient’s brain in an effort to reverse the stripping away of myelin, the protective sheath that surrounds nerve fibers in the spinal cord and brain. It was the first central nervous system transplantation to repair the myelin-forming cells in a patient with multiple sclerosis.

The purpose of this experiment was to determine whether the procedure is safe and has enough promise to justify future research,” said Timothy Vollmer, m.d., associate professor of neurology and principal investigator on the experiment.

Animal studies have found that Schwann cells, which make myelin in peripheral nerves, can replace oligodendrocytes, which make myelin in the brain and spinal cord. Vollmer and his team wanted to determine whether Schwann cells can not only survive in the human brain, but also wrap myelin around nerve fibers and restore normal function.

Over two days in July Vollmer’s team first isolated Schwann cells from the sural nerve in the patient’s ankle. Then, a neurosurgery team led by Dennis D. Spencer, m.d., ’76, University of California, San Diego, and the patient’s neurosurgeon, injected the cells into a previously identified multiple sclerosis lesion. For the next six months researchers will monitor the patient with both neuroimaging and functional assessments. Then surgeons will perform a biopsy to see whether the cells survived and made myelin.

The team included Jeffrey Ko (left), Stephen G. Waxman, m.d., ’72, and others. The research is funded by The Myelin Project in Washington, D.C.
**OUT DOWN SYNDROME**

**SIMPLE MEASUREMENTS RULE INSTEAD OF A NEEDLE,**

Yale researchers have developed an algorithm that allows physicians to gauge the risk of Down syndrome in fetuses without resorting to amniocentesis, an invasive procedure that could cause a miscarriage. Instead, physicians rely on what is called an ultrasonic biometry algorithm, which measures risk based on a number of factors, including information gathered by ultrasound — measurements of the fetus’s upper arm and skin at the back of the neck.

In a study published in the May issue of the American Journal of Obstetrics and Gynecology, Ray O. Bahado-Singh, m.d., associate professor of obstetrics and gynecology, reported that the algorithm proved accurate in almost 80 percent of cases. Having this assessment allows parents to determine whether to proceed with amniocentesis.

Down syndrome is a congenital disorder caused by an extra chromosome 21. Children with Down syndrome have mild to moderate mental retardation, shorter stature and flattened facial features. Women over 35 with amniocentesis.

 Babies over 35 have a higher risk of giving birth to a child with Down syndrome, but using age alone physicians detect only about one in five cases, said co-author Joshua A. Copel, m.d., professor of obstetrics and gynecology and pediatrics. “Using blood tests and ultrasound we apply adjustments to the mother’s age-related risk,” Copel said. “This would mean fewer amniocenteses and a higher percentage of abnormal babies identified.”

**JOBS AND BRAIN CANCER MAY BE LINKED**

Farm workers, waitresses and people who work with rubber or cleaning chemicals are at a higher risk for brain cancer, according to a study by Yale scientists published this spring in the journal Occupational and Environmental Medicine.

**PATHOLOGISTS SET NEW CRITERIA FOR CANCER PRECURSOR**

Pathologists tracking the progression of disease from acid reflux to esophageal inflammation to Barrett’s esophagus, a precursor of cancer, can’t always agree on how to evaluate biopsies. Now, at a national group of gastrointestinal pathologists founded by a Yale professor has developed new criteria for grading pre-malignant changes in cells, also referred to as dysplasia.

Criteria for grading dysplasia were established in 1988, but still led to inconsistent results among pathologists. “That grading decision,” said Marie E. Robert, m.d., associate professor of pathology, “is made by looking through a microscope at a slide of a biopsy. It is very subjective.”

Using their new criteria, Robert and 11 other gastrointestinal pathologists found that they agreed more often on categorizing dysplasia. Among the revisions they suggested was more attention to the location of atypical cells. Atypical epithelial cells on the surface of the mucosa are more predictive of future cancer than cells in the deep mucosa.

The new criteria is also sought to clarify the difference between low-grade dysplasia, which requires routine follow-up, and high-grade dysplasia, which usually prompts surgical resection. Robert said.

A follow-up study of patients found a correlation between diagnoses with the new criteria and cancer risk. “When we modified and discussed the criteria, the risk of developing cancer went up in a linear fashion, after earlier biopsy diagnoses of negative, low-grade and high-grade dysplasia,” Robert said. “That would argue that our new criteria are valid and can guide clinicians and patients on how they ought to be followed once these diagnoses are made.”

**LESSONS IN GERIATRIC MEDICINE**

The care of elderly patients is far more complex than treatment of younger people, yet clinicians too often ignore this difference. The medical school has received a $2 million grant from the Donald W. Reynolds Foundation to teach medical students how to care for the aging population. “With the elderly, any problem has many causes and consequences that need to be understood,” said Margaret A. Drickamer, m.d., associate professor of internal medicine and geriatrics at Yale, and lead investigator on the project. “It means asking more questions and asking different questions.”

Drickamer hopes to integrate geriatric medicine into existing curricula. “We don’t want to take away from existing programs,” she said. “We just want to make sure the concepts are taught.”

An algorithm developed by Ray Bahado-Singh and Joshua Copel uses data from ultrasounds and other measurements to gauge the risk of Down syndrome.
AIDS VACCINE CLEARS FIRST HURDLE

Liver virus is the vector for agent that works in monkeys; nasal administration seen as plus.

A vaccine that uses an attenuated live vector as a two for hIV proteins to keep infected monkeys free of more than a year, according to a team led by Yale scientists. The vaccine proteins, some infected with a highly pathogenic simian hIV virus for as long as 34 months, have not developed full-blown hIV and their viral loads have remained low. The vaccine shows promise in another area: it can be administered through nasal drops rather than by injection, making it more affordable and practical for use in developing countries, where hIV is taking its heaviest toll.

“Based on our results we think it is likely that this vaccine could be an effective hIV vaccine in humans,” said John K. Rose, Ph.D., professor of pathology and of cell biology. Rose and his wife, NinaF. Rose, Ph.D., an associate research scientist, led a team that included scientists at Yale, the Auron Diamond al’s Research Center, Tufts University, and the Gladstone Institute of Virology and Immunology. Their results were published in the September 7 issue of Cell and presented at al’s VACCINE 2001 Conference in Philadelphia in September.

The virus, vesicular stomatitis virus (vSV), is a preferred vector for vaccines because it provokes a strong immune response. Although never tested in humans, vSV has proved effective in animal models as a vector for influenza and measles vaccines. The combination of the virus and two hIV proteins called Env and Gag put the monkeys’ immune systems on high alert, making them more effective against hIV, John Rose said.

“IT is a very strong stimulator in both arms of the immune system—the antibodies and the cellular immune system,” he said. “This holds down the spread of the infection in the animals. There are fewer infected cells. It is less of a task for the immune system to hold the virus in check and the viral loads go down to very low or below detection.”

The ability to deliver the vaccine in drops rather than through needles, said Rose, is crucial in developing countries. “It would be impractical and very expensive to inject millions of people with hIV vaccines,” he said. “The vSV-based vaccine would be a cost-effective and equally successful alternative to other vaccines that have been tested.” In addition, the vaccine proved far more effective when administered nasally than when injected intramuscularly.

In two studies carried out over the past four years, the team vaccinated seven monkeys and left eight monkeys in a control group with no vaccination. All 15 monkeys were then infected with a hybrid of human and simian hIV viruses. “We found that seven out of the eight vaccinated monkeys developed hIV in an average of five months, while vaccinated monkeys had been hIV-free for up to 34 months,” Rose said.

Wyeth Lederle Products Corp. has licensed rights to the vector and is conducting further animal tests in collaboration with Yale scientists before proceeding to clinical trials.

IN A STUDY IN MICE, ADULT STEM CELLS REVEAL THEIR VERSATILITY

Stem cells derived from the bone marrow of adult mice, a Yale researcher and her colleagues have found, can create not only new bone marrow cells, but liver, lung, gastrointestinal and skin cells. “Thus far, this is the closest adult-derived stem cell to the embryonic stem cell, which can transform into any cell type in the body,” said Diane Krause, M.D., Ph.D., associate professor of laboratory medicine and pathology. Krause was lead author of the study, which was carried out by scientists from three institutions. Their study was published in the journal Cell in May.

The research built on the same group’s earlier experiments in mouse models that showed that bone marrow cells could generate new liver cells, including hepatocytes and cholangiocytes (Findings, Fall 2000 | Winter 2003). Krause and her colleagues then showed that this regeneration also occurs in humans. “However, we didn’t know if the bone marrow cell that could make liver was the same cell that could make blood,” Krause said. “We wanted to know what cell it was.”

ET CETERA . . .

NEW GENES FOR HYPERTENSION

A team of Yale scientists has identified mutations in two genes that cause a rare form of hypertension. The finding has also uncovered a previously unknown metabolic pathway governing blood pressure that could offer new targets for medications.

The finding, reported in the August 20 issue of Science, identifies genes on chromosomes 12 and 17. In their mutated form they can cause increased reabsorption of salt by the kidneys and impaired secretion of potassium and hydrogen ions. This leads to a rare form of hypertension called pseudohypoparathyroidism type II.

The principal investigator on the study was Richard P. Lifton, M.D., Ph.D., professor of genetics, medicine, and molecular biophysics and biochemistry and an investigator for the Howard Hughes Medical Institute.

AN HERBAL CLUE TO INFLAMMATION

An herb commonly used to treat migraine headaches inhibits a protein that causes inflammation, Yale pharmacologists have found. In an article published in the August issue of Chemistry & Biology, a team led by Craig Crews, M.D., Ph.D., associate professor of chemistry, pharmacology, and molecular, cellular and developmental biology, showed that a component of the herb feverfew targets a protein called 12kDa Kinase, which is responsible for inflammation.

“Now that we have identified an inhibitor of this protein,” said Crews, “that information can be used to develop additional inhibitors.”

A CASE OF HIDE AND SEEK?

Treated early, Lyme disease is usually cured with antibiotics, but the prolonged form of the disease can be more troublesome. Yale scientists have observed that while the Lyme spirochete is easily digested by immune cells in vitro, rare bacteria within the body can withstand the onslaught of the immune system, perhaps explaining the spirochete’s ability to survive long-term. Ruth R. Montgomery, Ph.D., set out with colleague Stephen Maksic, M. D., to determine whether the spirochete somehow weakened the immune system. Results of a study of mice published last June in the Journal of Infectious Diseases strongly suggested that this was not the case. With defects in leukocyte function all but ruled out, the team will look next at the other side of the equation: how the spirochete may be masking itself from immune surveillance.

This book evaluates whether recently formed health networks can generate the fiscal savings to provide greater access to and quality of health care despite the current threat of cutbacks in reimbursement from Medicare and managed-care plans. It concludes with a very timely and much needed discussion of how U.S. health networks might distill certain programs, services and facilities in the case of an almost inevitable economic downturn.

Quantitative Evaluation of HIV Prevention Programs edited by Edward H. Kaplan, ph. d., the William K. and Maria A. Beach Professor of Management Sciences, and professor of public health, and Ron Brookmeyer Yale University Press (New Haven), 2002

How successful are HIV prevention programs? Which HIV prevention programs are most cost effective? This programs are worth expending and which should be abandoned altogether? This book addresses the quantitative evaluation of HIV prevention programs, assessing the first time several different quantitative methods of evaluation.


A hub for health care
Schools can provide access to health care for children who might not otherwise see a doctor, former U.S. Surgeon General Joycelyn Elders, m. d., said during a visit to New Haven in early July. Speaking to teachers, principals, program directors and policymakers at the 11th annual conference of the School of the 21st Century (SC) initiative, Elders urged schools to establish clinics focusing on prevention. “You can’t educate people who are not healthy, and you certainly can’t keep people healthy if they’re not educated,” said Elders. Established in 1988, the SC initiative was founded by Edward F. Zigler, m. d., one of the principal architects of the federal Head Start Program, Sterling Professor of Psychology and a faculty member in the Child Study Center. More than 150 schools in 40 states have adopted the program, which transforms schools into multiservice centers providing a variety of resources for children, parents, teachers and child-care providers.


A hub for health care
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The Stranger in the Mirror: Dissociation—the Hidden Epidemic by Mariane Stansberg, m. d., former research associate in psychiatry, and Marlene Schnall Cliff Street Books (New York), 2001

In a handy, practical format, this book offers reliable information on the relevance, safety and effectiveness of various complementary and alternative therapies that are not typically considered in discussions of dissociation management but are in widespread use.


Based on Steinberg’s 18 years of research a...
After Flexner, a new start

In 1910, the medical school’s fate hung by a thread. The deep criticisms it weathered in a landmark report ultimately made it a much stronger institution.

by Pem McNerney

The Flexner Report of 1910 prompted Yale and many other medical schools in the United States to make fundamental changes. Author Abraham Flexner, above, recommended that Yale School of Medicine remain open but that it bolster its fund-raising and hire full-time faculty, among other improvements.

The release of the Flexner Report in 1910 was bad news for most of the nation’s medical schools. Commissioned by the Carnegie Foundation for the Advancement of Teaching to evaluate the ability of U.S. medical schools to train new doctors, consultant Abraham Flexner’s verdict was that most weren’t up to the task. He recommended that the vast majority of schools be shut down. In New England, he said, the only two worth saving were Yale and Harvard. And despite the tacit endorsement, the report singed out Yale’s thinly stretched faculty as a weak point. “The instructors ... are overworked, being called on to carry the routine work of extensive subjects in all their parts without adequate assistance. Under such circumstances, the work, however conscientious, is bound to be limited.” The report also recommended that the school obtain a larger permanent endowment.

The School of Medicine’s bleak condition at the turn of the century and its successful efforts to rehabilitate itself are the subject of Medicine at Yale, 1901–1955, the second in a series of exhibits at the Cushing/Whitney Medical Library marking the University’s Tercentennial this year. The exhibit, which has been adapted for the web, shows how, in the 1920s, the school transformed itself from a mediocre institution with part-time faculty and limited resources into one of the nation’s top medical schools. With a full-time staff, new facilities and many new departments, including the innovative and controversial Institute of Human Relations, the school generated enough momentum in the 1920s to survive both the Depression and World War II intact.

The Flexner Report’s grim assessment of Yale’s resources and facilities came as no great surprise to the school, which had been struggling for its survival since the 1880s. Herbert E. Smith, dean from 1885 to 1900, had made some improvements. He tightened entrance requirements, expanded the curriculum and made efforts to establish closer ties with New Haven Hospital. His successor, George Blummer, dean from 1900 to 1920, was able to establish a sorely needed, more functional system for key faculty, providing them with a full-time salary for teaching and research. He also oversaw the growth of the endowment fund and forged an agreement with New Haven Hospital that allowed the school to take charge of the wards and use them for medical education. One of Blummer’s proudest achievements was the establishment of the Department of Public Health in 1915, with Charles Edward Amory Window as its founding chair. In 1920, Milton C. Winternitz became dean. He oversaw the construction of the Starling Hall of Medicine, the expansion of clinical facilities and the establishment of several departments, including the Department of Pediatrics (1922), the Department of Obstetrics and Gynecology (1921) and the Psychiatry Group (1931). During his tenure, the Department of Surgery was moved to a full-time basis and the Yale System of Medical Education was established. Under the Yale System, medical students were treated like graduate students, required course exams were eliminated and electives were encouraged. The Institute of Human Relations, specializing in interdisciplinary research in medicine, law and the social sciences, was created in 1933. According to the exhibit text, “Winternitz sparked strong emotions in his colleagues. To some he was brilliant, bold, and ‘a steam engine in pants,’ and to others he was an insusceptible ‘martinet,’ a Napoleon, and an anti-Semitic” though he was Jewish himself. In 1935 he was forced to step down from his post as dean, continuing on as chair of pathology until his retirement in 1950.

Yale had three more deans during the first half of the century: Stanhope Bayne-Jones (1905–1940), Francis Gilman Blake (1941–1947) and Cyril Norman Hugh Long (1947–1952). Among other notable accomplishments, they succeeded in getting the medical school on solid financial ground so that it could continue to grow following World War II.

In 1964, the Yale School of Medicine admitted women students for the first time. Louise Farnam was one of two women to graduate in 1965. George Blummer, dean from 1920 to 1935, presided over the boom years of the medical school following World War I, when it entered as one of the top medical schools in the country. Winternitz embarked on a campaign of building buildings, hiring faculty, organizing departments and raising money to finance it all. The son of an immigrant doctor, Winternitz was controversial and evoked strong feelings among his colleagues. He was forced to step down as dean in 1935, but continued on as chair of pathology until his retirement in 1950.

More on the Web
To view the online exhibit Medicine at Yale, 1901–1951, please visit our website and select extras.
Sharks, salt
(and a taste of lobster)

An intensive week at the bench in Maine introduces students to modern lab strategies and techniques, ancient DNA and a clambake to write home about.

Text and photographs by John Curtis

A slice of a shark’s rectal gland captures the attention of Jenny Blair, Vicash Dixwold and Dena Springer as Ignacio Gimenez, a postdoctoral fellow in physiology, guides them through an experiment at the Mt. Desert Island Biological Laboratory in June. The Yale students isolated a protein in the gland, then measured its response to phosphorylation.
Few medical students can say that, as part of their education, they plucked a writhing dogfish shark from a pool of water. Or that they ended their first year by seeking clues to human disease in the organs of a fish that reached its evolutionary peak more than 300 million years ago.

This past June that pool of sharks lured about two dozen Yale students to Salisbury Cove, Maine, just a few miles from Bar Harbor. For more than a century, scientists at the Mt. Desert Island Biological Laboratory here have explored the genes shared by fish and humans. For about half its lifetime, the laboratory has had strong ties to the School of Medicine, a relationship that began in the 1950s, when Franklin Epstein, m.d., h.s.’47, professor of medicine, began bringing residents and fellows to Maine. In June 2000, for the first time, medical students arrived for a week’s training in bench research. This year another group of students repeated the Intensive Pedagogical Experience, a program designed to introduce them to the strategies and techniques of laboratory science and to encourage them in careers as physician-scientists. Most of the students arriving in June had just completed their first year of medical school; the group also included a student who began med school this fall.

In the course of their week on Mt. Desert Island, the students cloned genes, learned to synthesize DNA by means of polymerase chain reaction and generated copies of proteins by inserting RNA into frog eggs. They also learned the difference between Western blots, used to find specific proteins, and Southern and Northern blots, used to find the DNA and RNA for specific genes.

Rupali Gandhi, who is beginning her second year at Yale this fall, majored in biology as an undergraduate, then went on to get a law degree at Yale before taking up medicine. "I hope to come away from this course with a better understanding of a lot of research methods so that the next time I read a journal article my eyes won’t glaze over the methods section," she said, sitting on a porch outside one of the many laboratory buildings scattered throughout the forest. Understanding research strategies and gaining familiarity with the scientific method are among the goals of the course, according to its director.

“The idea of rigorous pursuit of a question and a clear hypothesis is applicable to all that students do in research at Yale,” said John N. Forrest, m.d., h.s.’67, who heads the Office of Student Research at the medical school and is director of the Mt. Desert Island Biological Laboratory, where he has spent the last 32 summers.

Long before the first group of Yale students traveled to Maine, the notion of an intensive laboratory experience was brewing in the mind of Dean David A. Kessler, m.d. As an undergraduate at Amherst College, he spent four weeks one summer at the Woods Hole Marine Biological Laboratory. The time he spent studying macrophage inhibition factors in sea urchins served as a model for the program in Maine. Kessler wanted to provide students with both hands-on laboratory experience and a chance to interact closely with faculty. "You get to see things you just don’t see sitting in a lecture hall," he said. "This is what education should be." And holding the course on Mt. Desert Island freed students and faculty from the day-to-day distractions of being on campus.
Sharks, salt [and a taste of lobster]

Forrest scheduled the course for early June, after students have completed their medical school course work and before the lab’s high season in July and August, when its year-round population of 17 staff members swells to more than 200 principal investigators, postdocs, graduate students and laboratory technicians.

Amidst the laboratory’s 3.5 acres of poplar, pine, spruce and cedar forest, the hierarchy that typically rules academia takes a sabbatical. First of all, the laboratory, with its shingled and weathered buildings in the woods, looks more like a fishing camp than a research center for top scientists from more than 50 institutions. But enter those buildings and you’ll see they’ve filled not with lobster pots and fishnets, but with beakers, pipettes, computers, centrifuges and a gene sequencer. Dress is informal. As often as not, students and faculty wear T-shirts, shorts and sandals. They spend most of their waking hours together. And, most troubling for some students, only first names are used. “We all know him as Dr. Forrest because he’s the head of research,” said student Dena Springer. “We come here and he’s John.”

At the heart of the students’ experiments is the rectal gland, an organ unique to sharks and other fish. Local fishermen provide a regular supply of spiny dogfish sharks, also known as Squalus acanthias, a relatively benign member of the shark order. Between 16 and 20 inches long, they are decidedly passive compared to their great-white cousins. Students say these fish will vade a regular supply of spiny dogfish sharks, also known as Squalus acanthias, a relatively benign member of the shark order. Between 16 and 20 inches long, they are decidedly passive compared to their great-white cousins. Students say these fish will

Examining a fish’s ability to control its salt may seem a highly esoteric subject, but the course offers a chance to understand standing cystic fibrosis, the most common fatal childhood disease and one that is also concerned with salt imbalance. It is caused by a genetic disorder, the malfunction of a protein called the cftr chloride channel, which renders the body unable to regulate chloride transport. Without the proper functioning of this protein, a sticky mucous secretion develops, clogging lungs, sinuses and the digestive system.

Working in four groups of six, the students approach the gland from various perspectives. Over the course of a week they try to answer these and other questions: What is the function of the rectal gland in the shark? How is secretion by the gland regulated by known agents and second messengers? What is the function of cftr? Can we determine Na-K-Cl cotransporter activation in an isolated cell preparation? What is the importance of single nucleotide polymorphisms in the post-genome era?

Students may look at the entire organ, measuring its function with agents such as barium, forskolin or IBMX, which inhibit or stimulate chloride transport. For another experiment, working with tissue from the gland, they isolate a protein and try to turn on and off its capacity to transport sodium, potassium and chloride. They may phosphorylate the protein and look for signs of activity. When they look through a confocal microscope, the students expect to see a lot of green, a sign that phosphorylation has activated the cotransporter protein. They also take the cftr chloride channels they’ve generated in frog eggs and measure their electrical activity. Continuing the experiment, they add hormones to open and close the channels.

The science behind the experiments was complex, and at times the mechanics could be demanding and repetitive. One rainy afternoon medical student Jenny Blair watched as a shark’s salt gland excreted liquid into a narrow-bore pipette several inches long. When the pipette filled, every few minutes or every few seconds, depending on whether chemical agents were involved, she inserted a new pipette into tubing coming from the gland, while others on her team measured the amount of liquid, then determined how much chloride it contained. Upon completing the experiment, they calculated the gland’s ability to excrete chloride under the conditions studied.

Part of the students’ fascination comes from knowing that another team in another lab or rotation will pick up on their experiments. “We took the body parts of a shark and extracted rna from them,” said student Benjamin Negn, describing a typical research sequence. “Then we passed the baton on to the next group. They’re turning their rna into dna. The final group is using polymerase chain reaction of the dna to identify what it is.”

Niya Jones and Bao Duong were part of the second team in the sequence Negn described. They learned how to manipulate a pipette to insert shark dna into an agarose gel. They were filtering the dna by size, looking for the genes related to a family of proteins that regulate chloride transport. Steve Aller, a doctoral candidate at Yale, guided them through the process, teaching them how to hold the pipettes so the dna slips into a well in the gel without smearing.

When, at the end of their experiment, they found a set of small genes they could not identify, Jones and Duong passed them off for further research to the next team in the rotation. “If it’s a subunit of the cftr channel or an unrelated protein, it would be the use of a pipette for an experiment with shark dna.
interesting to see," said Spencer Epps, who planned to compare the genes to those in an online database at the National Institutes of Health.

Not all the experiments yield clear results. In presenting their findings, students were refreshingly honest about the success and failures of their experiments, as well as the unanswered questions. "We don't have wild-type data," said one student whose team explored mutations in ion channels, "because it got messed up." "The sequencing did not work," said a member of Epps's group, which had hoped to identify unknown genes, "and we're not sure why." Most experiments proved successful, insofar as the students noted patterns of behavior in the way cells responded to stimulants and inhibitors. For example, John Koethe explained the slopes and valleys on a graph that tracked the rectal gland's response to different agents. "They show barium inhibition, recovery then inhibition," he said. Another group working with rectal gland slices and tubules found that forskolin and bimx activated the chloride channel, leading to chloride secretion. Working with the whole gland, one team reported inconclusive results of their experiment; a high dose of potassium inhibited chloride secretion but a low dose yielded mixed results that offered no firm conclusions as to its effect.

The experiments conducted here are a natural outgrowth of the laboratory's focus on the physiology of marine and human organisms. Sharks, for example, reached evolutionary perfection between 300 million and 400 million years ago. For high school students from surrounding areas, their genome is about 70 percent identical to that of humans. "Humans adopted many of the successful systems they evolved," said James L. Boyer, Ensign Professor of Medicine and director of the Yale Liver Center, who heads the Mt. Desert Island Biological Laboratory's Medicine; a high dose of potassium inhibited chloride secretion but a low dose yielded mixed results that offered no firm conclusions as to its effect.

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A world
OF DIFFERENCE

Yale’s International Health Program sends young doctors around the globe to provide needed care—and learn the basics of a simpler medicine.

BY CATHY SHUFRO

IMAGES COURTESY MICHÉLE BARRY, FRANK BIA, JOEL GALLANT, DELIA RADOVICH AND PHOTODISC
Ramona Farid, M.D., knew she wasn’t in New Haven anymore the night she found herself on a hospital patio pouring a patient’s urine on an anthill. She was testing for glucose.

If she’d been at Yale, Farid wouldn’t have had to think twice about how to follow the progress of a 16-year-old girl in diabetic ketoacidosis, or DKA; she would simply have ordered finger sticks at two-hour intervals and checked the patient’s blood for glucose using a glucose monitor. But this was rural Haiti, where the second-year resident was working for a month with Yale’s International Health Program (IHP). It was 2 a.m., and there wasn’t a test strip to be found at Hôpital Albert Schweitzer.

“I said, ‘How the heck am I supposed to manage DKA without Chemstrips?’” recalled Farid.

Finding low-tech (or no-tech) strategies for diagnosing and treating patients is one of the challenges for residents like Farid who take part in the Yale IHP. Since 1981, the popular program has sent residents in internal and emergency medicine to serve more than 300 rotations overseas or in Indian Health Service hospitals in the United States. This year, 40 of the 303 residents in internal medicine will spend four to eight weeks in locales ranging from Alaska to Zimbabwe. They will be the first to be sponsored by a grant from Johnson & Johnson that will fund the 20-year-old program and allow it to expand.

That night in Haiti, Farid realized enough about diabetes to monitor her patient’s ketoacidosis without Chemstrips. Taking on the phone with the Haitian attending, she saw the logic behind the anthill approach. “In a patient in DKA, glucose levels would be high not only in blood, but also in urine. By observing how many ants were attracted by the sugar in the girl’s urine compared to urine from someone without diabetes, Farid could track the decline in the patient’s glucose levels. And so, for the rest of the night, she went out to the anthill with urine samples every two hours. At 8 a.m., the ants stopped coming. Farid took the girl off the insulin drip and sent her home with injectable insulin.

The insight that Farid gained in Haiti — recognizing that she had useful knowledge of a disease independent of expensive technology — is one of the goals of the IHP, according to Frank J. Bia, M.D., its co-founder with Michele Barry, M.D., ’77. With the extensive use of diagnostic radiology and laboratory testing, said Bia, young doctors today “often are not allowed to think through a diagnosis. This diagnosis might be handed to them on a silver platter, or an MRI scan.” Overseas, residents “have to go back to actually listening and touching. We feel these are very important skills to bring back to the art of being a doctor.”

In a retrospective study of the program, residents reported that by practicing back-to-basics medicine they gained confidence in their ability to do physical examinations and came to value them more. The study by Robert Wood Johnson Clinical Scholar Anu J. Gupta, M.D., ’94, M.S., ’00, was published recently in The American Journal of Tropical Medicine and Hygiene.

Residents in the program also have the chance to try procedures they rarely get to practice at home. At the Alaska Native Medical Center in Anchorage, second-year resident Walter Lin, M.D., helped with a bone marrow biopsy and saw internists take other tasks usually reserved for specialists. In South Africa and in Cuba, resident Delia Radovich, M.D., ’91, found that practicing medicine where care is free and resources are limited was liberating. She did not have to document every move she made, haggle with insurers or track myriad confirmatory tests.

Working in a medically underserved area, she said, “takes you a better doctor just by realizing the world doesn’t work the same way the United States works. It makes you more human. It pulls you out of your daily grind, and it brings you back to the real reason you chose medicine, or should have chosen medicine taking care of patients.”

The physician’s obligation to care for patients provides the motive for the International Health Program, said Bia. “It’s a professional ethic that guides the program. You have a social contract that extends beyond the walls of the hospital, and which others do not have. You have taken the Hippocratic Oath. It says, ‘Aid the Weak with the Protection of your Life and Honor.’”

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The experience is opening people’s minds to underserved areas around the world, not only overseas but also in New Haven. Alumni of the program have chosen careers reflecting this vision. Gupta’s study found that the 330 Yale residents who went abroad between 1982 and 1996 were more likely than their counterparts to practice in public health settings and more likely to care for indigent patients, immigrants, substance abusers and patients with HIV. For instance, among the doctors in this study who now practice in public health settings, 10 had participated in the International Health Program, while two had not. Among those in the study with a substantial number of HIV-positive patients (more than 20 percent), 30 had gone abroad, while 33 had not.

Joel E. Gallant, M.D., M.P.H., ’89, fits this profile. Having elected a rotation in Haiti in 1987 and in Tanzania and Zimbabwe in 1988, he now serves as associate director of the Johns Hopkins AIDS Service. “It was always my goal to be working with underserved populations in developing countries,” said Gallant. “However, my training at Yale and at Hopkins showed me that there were underserved populations on our doorstep, and that was especially true with AIDS.”

The fact that many participants in the program go on to care for marginalized patients appealed to the contributions committee at Johnson & Johnson, according to Conrad Person, its director of international programs. The New Jersey company’s credo calls for community and global responsibility. “This program fits,” said Person. “Yale was able to demonstrate that people who participated in this program were more likely to develop compassion in the practices they developed years later. This is an exciting program that expands the perspectives of people who are very likely to be leaders in the world of health care in the years to come.”

This year’s grant from Johnson & Johnson will send 40 residents to Indian Health Service hospitals in Arizona, New Mexico and Alaska and to 12 countries including Fiji, India, Russia, Israel, Brazil, China and Nepal. Next year, the gift will allow the program to expand to include residents from other medical schools as well as physicians with established practices. Bia estimates that the grant will come to about $30,000 annually, covering expenses formerly paid for by the Department of Medicine and income from a travelers’ clinic run by Barry and Bia. Yale New Haven Hospital will continue to pay residents’ salaries while they are away.

For Radovich, now a fellow in hematologic oncology at Memorial Sloan-Kettering Cancer Center, the experience of working abroad was invaluable. “It chose Yale for Yale, not even knowing that this program was in place. But I think people should come to Yale in droves, knowing this is an option.”

September 11 hasn’t diminished the program’s ambitions; if anything, it has set the bar higher. Barry told a group of students attending the poster session for the Dow’s International Health Student Travel Fellowship Program in October, “There is a whole world out there that is going to need you even more.”

Farid’s words to her medical students remained with them. “I just hope you keep your global vision.”

AMY SHUFRO, contributing editor of Yale Medicine and a tutor in the Bass Writing Program at Yale.

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Type 2 diabetes poses alarming health risks as obesity soars and exercise is crowded from modern life. Yale investigators are seeking better ways to prevent and treat the disease and to understand the science of fat.
For a nation obsessed with fitness, it’s a small wonder that so many Americans manage to keep gaining weight. Despite an ever-growing choice of diet products and weight-loss programs, more and more Americans are losing the struggle against an expanding girth—or not fighting it at all. According to the Centers for Disease Control and Prevention, rates of obesity surged 60 percent during the past decade and, today, one in five Americans is considered obese, or 30 percent above his or her ideal weight.

People who are serious about actively battling obesity have generally turned to fitness instructors or nutritionists. But at Yale, fat is also the stuff of serious science, pursued by nearly 300 epidemiologists, pediatricians, endocrinologists, biologists, nurses, biochemists and psychologists, among others. They are all part of the Yale Diabetes Endocrinology Research Center, led by Robert S. Sherwin, m.d., the C.N.H. Long Professor of Medicine and past president of the American Diabetes Association. Founded in 1993 with a grant from the National Institute of Diabetes and Digestive and Kidney Diseases, the Yale diabetes center provides the infrastructure for an active interdisciplinary team representing 16 departments. Its mission is not to trim the American waistline but to find ways to prevent and treat an often-serious consequence of obesity, type 2 diabetes mellitus.

Type 2 diabetes occurs when beta cells in the pancreas lose their ability to produce enough insulin to compensate for defects in glucose metabolism. Unlike type 1 diabetes, an autoimmune disease that destroys the beta cells and all of the body’s insulin-making ability, type 2 diabetes leaves patients capable of producing insulin but unable to use it effectively. This can result in kidney and heart disease, stroke, blindness, nerve damage and loss of limbs. In 1997, the American Diabetes Association (a.d.a.) estimated that 36 million Americans had diabetes. According to Sherwin, the number has increased by at least 6 percent a year since then, largely in tandem with the rise in obesity.

Worse, type 2 diabetes, long thought of as an adults-only illness, is now striking increasing numbers of young people, particularly Native Americans, African-Americans, Asians and Latinos. “We are seeing obesity running rampant, particularly in young adults,” says Sherwin. “It’s a major health problem that has gotten increasingly worse in the past five years.”

The Yale group has focused its efforts on understanding the biology of type 2 diabetes and on crafting strategies to prevent its occurrence in key groups of patients at risk for the disease. These approaches draw in a diverse group of investigators who are interested in everything from the biochemical pathways of glucose metabolism to the best ways to encourage at-risk children and older adults to exercise and follow a healthy diet.

IN VIVO BIOCHEMISTRY

Gerald I. Shulman, m.d., ph. d., has spent the past 15 years exploring the cellular mechanisms of insulin resistance, the defect in the body’s ability to use insulin that characterizes type 2 diabetes. Insulin resistance has been shown to be the best predictor for whether or not an individual with a family history of type 2 diabetes will go on to develop diabetes. Recently, his team proposed a new mechanism to explain how an excess of fatty acids in the bloodstream increases the risk of diabetes by interfering with glucose metabolism. “Clearly too much fat is bad for you and somehow it interferes with insulin’s ability to stimulate glucose uptake into skeletal muscle. We wanted to know how,” says Shulman. To find out, he and collaborators including Douglas L. Rothman, ph. d., Kitt F. Petersen, m.d., Robert G. Shulman, ph. d. (no relation to Gerald) and Gary W. Clune, ph. d., have used the tools of nuclear magnetic resonance (nmr) spectroscopy to perform what Shulman calls “in vivo biochemistry in real time.” Their techniques allow researchers to measure metabolic changes noninvasively and with much greater sensitivity than was possible before.

“In the old days, we would have had to perform muscle biopsies to assess the concentration of a metabolite in a particular tissue. Even then we wouldn’t have had nearly as clear a picture of what was going on inside the cell because a cell doesn’t behave the same once you remove it from the body,” says Shulman, the associate director of the Yale Diabetes Endocrinology Research Center, professor of medicine and of cellular and molecular physiology, and a Howard Hughes Medical Institute investigator. An example of the power of the nmr technique was recently demonstrated in a study in which his group used it to measure the amount of fat inside the muscle cells of normal volunteers. They found that higher levels of intracellular fat are the best indicator of whether or not an individual is insulin resistant.

In order to determine the way in which fatty acids trigger the chemical defects that interfere with insulin’s ability to stimulate glucose transport, the Yale researchers infused fatty acids into healthy volunteers and found that they could induce insulin resistance temporarily within five to six hours—demonstrating an inverse link between the presence of fatty acids and the body’s ability to metabolize glucose. In a subsequent study the Yale team found that excess fatty acids block insulin’s ability to activate phosphoinositols 3-kinase, a key enzyme responsible for mediating the effects of insulin.

For older adults, is moderate-intensity exercise sufficient to lower the risk or severity of diabetes? Must one exercise a little bit every day or is one intense training session a week just as good?

Loretta di Pietro

Robert Sherwin

A tax on fat? The rise in obesity around the country has led a number of investigators to seek solutions in the realm of public policy. Among those is Kelly D. Brownell, Ph. D., director of the Yale Center for Eating and Weight Disorders, who advocates a six-step solution that would, among other measures, impose a tax on foods of poor nutritional quality.

While the idea of a “fat tax” has raised eyebrows (and the ire of many a conservative talk-show host concerned about limits on our right to eat whatever we want), it makes perfect sense to Brownell, a professor of psychology and of epidemiology and public health. “We see a health system far more focused on treatment than on prevention of obesity. He argues that “for every person we successfully treat and remove from the obese population, there are thousands more entering it.” In addition to taxing junk foods, his plan calls for publicly financing recreation centers and bike paths, regulating food advertising aimed at children, banning fast foods and soft drinks in schools, subsidizing healthy foods, and incorporating nutrition education in school lunch programs. “I think we have been obsessed with the biology and missed the obvious,” says Brownell. “It’s the humble food and lack of physical activity that are causing the problem.”
An epidemic in the making

Sonia Caprio

There have never been so many obese children. That is not to say that all these children will become diabetic—because it’s not too late.

Caprio, with people vulnerable to the disease, especially children. Research that leads to new drugs, clinicians are working directly on hormonal regulation and sugar and fat metabolism. Partici-

clearly that exercise training can reverse the major defect respon-

sible for insulin resistance in these individuals,” says Shulman, “and that it is likely to be an effective means in preventing or even reversing type 2 diabetes.”

AN AGGRESSIVE APPROACH TO TREATMENT

While researchers including Shulman are doing the kind of basic research that leads to new drugs, clinicians are working directly with people vulnerable to the disease, especially children. “There have never been so many obese children,” says Sonia Caprio, M.D., associate professor of pediatrics in the section of endocrinology. She has shown that excess weight clearly carries with it the risk of type 2 diabetes. Last year at the ADA meeting in San Antonio, Caprio reported that 18 percent of 380 children she tested during the course of treatment for weight disorders had impaired glucose tolerance. “That is not to say that all these children will become diabetic—because it’s not too late,” she says. “If they do improve their weight and increase exercise, they can prevent it.”

Still, a decade ago it was rare for more than 5 percent of all pediatric diabetes cases to manifest themselves in the type 2 form of the disease; most children had type 1 diabetes. Today, in some clinics that number has soared as high as 40 percent, according to Caprio. The phenomenon is so new that epidemiologists haven’t yet compiled national statistics by age. To understand what is happening, Caprio began a five-year study last year to deter-

mine the metabolic reasons behind the explosion of new cases of type 2 diabetes in children. “We want to learn more about the pathway and where the defect is,” she says.

Meanwhile, the race is on to find better ways to treat this new subset of patients before complications set in. Because people with type 2 diabetes usually develop it in middle age, complications often do not arise until their 60s or 70s. For the pediatric patients, the prospect of kidney failure or cardiovascular disease may come decades earlier, in their 30s or 40s.

In August, Caprio was awarded a $3.5 million grant over seven years as the principal investigator at Yale for a multicenter trial to compare standard medical therapies such as insulin and glu-

The women are divided into three groups. One group does high-intensity aerobic training, jogging on mini-trampolines at about 85 percent of their maximum capacity as measured by heart rate. The second group jogs at moderate intensity. The third group, considered the placebo group, does stretching, tai chi or yoga. The mini-trampolines provide aerobic exercise without.

Clearly too much fat is bad for you and somehow it interferes with insulin’s ability to stimulate glucose uptake into skeletal muscle. We wanted to know how.

Gerald Shulman
the jarring impact of running on the ground. About five women can work out at a time, which di Pietro says makes the routine more fun and motivates the women to continue exercising when the study is completed.

Fat in the abdominal area, which increases postmenopausally due to the drop in sex hormones, is linked to an increased risk of diabetes, says di Pietro, who is expanding the study to senior centers in New Haven and West Haven. These fat deposits, the deep kind that cover tissues within the abdominal cavity, are much more metabolically active than fat cells in the thighs and buttocks. In addition, there is a decline in both the quantity and much more metabolically active than fat cells in the thighs and buttocks. In addition, there is a decline in both the quantity and

1. In any dieter knows, gaining weight is a breeze compared to exercise a little bit every day or is one intense training session a week just as good?

FIGHTING EVOLUTION

As any dieter knows, gaining weight is a breeze compared to losing it. The reason, as is becoming increasingly apparent, has more to do with the evolution of the human species than with gluttony. Humans evolved in a dusty species because of an inherited ability to present starvation, says Sherwin. “We evolved on a planet where food was scarce and you had to work hard to get it. You needed a gene pool to hold onto calories.” In other words, those who survived long enough to produce a spring were able to pass along their calorie-hoarding genes. Those who dropped pounds easily died young. That was good for the survival of the species but is frustrating for those trying to lose weight today.

Ronald S. Duman, ph d., was appointed the Elizabeth Jameson Professor of Psychiatry. He has been on the Yale faculty since 1988, most recently as a professor of psychiatry and pharmacology, and has worked on characterizing the molecular and cellular mechanisms that mediate the long-term effects of psychotropic drugs and stress. His research suggests that antidepressants increase the survival and health of neurons and alter their synaptic architecture. Duman’s laboratory has also identified several neuropeptide receptors that are expressed in drug reward and craving.

Dean of the Graduate School of Arts and Sciences Susan Hockfield, ph d., was named the William Edward Gilbert Professor of Neurobiology. She joined the faculty in the Section of Neurobiology at the medical school in 1985 and has served as dean of the graduate school since 1998, overseeing the academic and administrative policies of the school, its 2,300 students and 750 faculty. Hockfield has sought to improve the quality of life for graduate students and increase opportunities for informal interaction between faculty and students. Her research work has looked at the molecular substrates involved in brain development, and she discovered a protein in the space around cells that is involved in early development and may play a role in brain tumors.

G. Shirleen Roeder, ph d., was appoint- ed the Eugene Higgins Professor of Molecular, Cellular, and Developmental Biology. Also a professor of genetics, he was part of a Yale team that recently fully characterized the function of the yeast genome. She has studied the process of metalloprotein interactions and characterizing yeast mutants defective in the process. She was named a Howard Hughes Medical Institute investigator in 1997. Roeder has been on the Yale faculty since 1981, and her work has appeared in the journals Cell and Science, among others.

Peter Salovey, ph d., a professor of epidemiology and public health and chair of the Department of Psychology, was named the Chris Argyris Professor of Psychology. He directs the Health, Emotion, and Behavior Laboratory and with John D. Mayer coined the term “emotional intelli- gence” to describe how people understand, manage and use their feelings. He has focused on how feelings facilitate adaptive cognitive and behavioral func- tions for humans and cancer. He is a deputy director of the Yale Center for Interdisciplinary Research on Aids.

Robert M. Weiss, m.d., was named the Donald Guthrie Professor of Surgery. He is a specialist in pediatric urology and urologic surgery and was listed in the latest edition of “Best Doctors in America: Northeast Region.” His research has covered topics from the role of nitric oxide in urinary tract infections and the bio-chemical and functional changes in the bladders of diabetics to the use of pulse-Doppler sonography in the diagnosis of urinary tract obstruction in children. He has been at Yale since 1967 and has served as chair of the Department of Surgery.

Robert Weiss

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Helping, and Learning, Through Disaster Relief in India

After an earthquake and as many as 60,000 deaths, Yale students and physicians help shore up health system.

Midway through their 10-day trip to western India in March to help with earthquake relief efforts, a team of Yale students and physicians visited the Children's Hospital in Bhuj, a city near the earthquake's epicenter. Shantiiben Patel, M.D., the hospital director, had set up tents outside the damaged building and was seeing patients when the team arrived. "She had been working six weeks straight, day and night," said Raj Krishnamurthy, M.D., who practices internal medicine at the VA hospital in West Haven and was a preceptor for the team. "She didn't have a day off. She was the only pediatrician in the whole area."

Patel quickly put the Yale team to work seeing outpatient patients while she tended to the neonatal intensive care unit in one of the many tents on the street. Over the next four hours the five students and their two preceptors tended to about 25 children, most suffering from diarrhea, dehydration, upper respiratory tract infections, malnutrition and urinary tract infections.

The earthquake that struck the western Indian region of Kachchh, on January 26, measured 7.9 on the Richter scale. Estimates of the death toll vary with the government estimating between 20,000 and 30,000 deaths and relief workers saying as many as 60,000 people may have died. The Yale team, made up of five medical students, a public health student and two physicians, arrived six weeks later to scenes of rubble and ruin. They also found an already fragile health care system in shambles.

In New Haven, students' initial response was a fund-raising drive that netted about $1,000 for earthquake relief. The students wanted to do more and approached Dean David A. Kessler, M.D., who agreed to send six students to India. It was up to the students to organize the trip. Seventeen students applied to go, and six, all but one of Indian heritage, were chosen through an application process. After securing their preceptors—Krishnamurthy and David Litvak, M.D., a third-year resident in internal medicine—and finding a nongovernmental organization to work with, the students were on their way. Upon their return, the students filed a report with the dean's office.

Kachchh is 20,000 square miles of plains, desert and salt flats bounded on the north by Pakistan and on the south by the Arabian Sea. Most of its inhabitants farm grains, cotton and lentils. Some work in limestone, marble and gypsum mines. In recent years the region has suffered two droughts and a cyclone. "It's a very difficult state to live in as it is," said student Simran Singh.

The team's guide to the region and its medical needs was Anupam Banerjee, M.D., an intern in India fresh out of medical school who had begun a term of service in Kachchh just after the earthquake hit. Banerjee, in turn, was working with the Shrujan Trust, an organization founded in 1969 to provide famine relief. The trust branched out into economic aid, providing medical care to villages. Their diagnostic and primary care included diabetes and hypertension screenings at a health camp at Shrujan. When it was time to leave, team members felt they had contributed something of value to the relief effort. The presence of the students and physicians on the medical van allowed more patients to be seen. Their survey left health workers a tool for predicting medical care to villages. Their report left health workers a tool for predicting medical care to villages. Their diabetes and hypertension screenings were the first for many patients and included follow-up via the mobile unit. And they established a program for children that others would continue after they left.

The students arrived at the Shrujan compound about 20 miles west of the city of Bhuj ready to work, despite a 36-hour trip from New Haven and a 10-and-a-half-hour time difference. Their new home was a one-room, thatched-roof hut with a single bed. (Most of the team slept on the floor or outdoors in their sleeping bags.) The next day half the team joined Banerjee on the medical van, while the other half went to the nearby village of Ghada to organize activities for schoolchildren. Although several members of the group spoke Hindi and one spoke Gujarati, language remained a problem in this country with more than 800 dialects. The dialect spoken in Kachchh was at times incomprehensible to the one Gujarati speaker on the team, Rupal Badani, a third-year medical student. Nevertheless, because of their knowledge of Indian languages and with the help of interpreters, the students managed to communicate.

Within a few days of their arrival, the team undertook a health assessment for Ghada, looking into nutritional patterns and access to health care, prenatal care and primary care. They also organized diabetes and hypertension screenings at a health camp at Shrujan. When it was time to leave, team members felt they had contributed something of value to health care in Kachchh just after the earthquake hit. Banerjee, in turn, was working with the Shrujan Trust, an organization founded in 1969 to provide famine relief. The trust branched out into economic aid, providing medical care to villages. Their diabetes and hypertension screenings were the first for many patients and included follow-up via the mobile unit. And they established a program for children that others would continue after they left. They also returned to New Haven with valuable experience, having been able to participate in emergency and primary care in a remote setting with limited resources. "We felt like we were doing something for someone, but we were also really learning," said third-year student Vivek Murthy.

The epicenter of the earthquake struck near Bhuj, the capital of Kachchh, and left much of the city in ruins.
For 500 Alumni and Their Guests, A Return to New Haven

Congress Avenue Building, brain research, admissions process are the focus of 2001 reunion.

At this year’s reunion, alumni donned hard hats for a tour of the Congress Avenue Building and put on their thinking caps for a seminar on admissions that asked them to decide the fate of a hypothetical medical school applicant.

More than 500 alumni and their guests attended reunion, which started Friday, June 1, with a discussion of the admissions process, a welcome from Dean David A. Kessler, m.d., and the traditional evening clambake. Across town, at the New Haven Lawn Club, alumni in public health were honored for their service to their communities.

The admissions discussion Friday afternoon in the Jane Ellen Hope Building included an interactive exercise that elicited the audience a chance to review the qualifications of various applicants and make their own selections.

The next day’s discussion turned to “The Last Frontier: Understanding the Brain, Curing its Disorders,” with a panel that comprised Bennett A. Shaywitz, m.d., professor of pediatrics and neurology and in the Child Study Center; Patricia Goldman-Rakic, m.d., the Eugene Higgin’s Professor of Neuropsychiatry and Psychiatry and Neurology, J. Ery D. Kocis, ph.d., professor of neurology and neurobiology; Dennis D. Spencer, m.d., chair and the Harvey and Kate Cushing Professor of Neurosurgery; and Stephen G. Waxman, m.d., ph.d., chair and professor of neurology.

The results would dismay the man as our maestro, and perhaps no one could! Non sede! Non sede! The growth of the physical facilities and the size, diversity of age and life experiences.

The highlight of our 55th reunion was the traditional gathering at Evelyn and Marty Gordon’s beautiful home on Linden Lake in Branford. As always, the refreshments were lavish and the entertainment began with videotapes from previous reunions as far back as our 40th. It reminded us that we haven’t changed since then except, perhaps, in appearance. What Miami and Judy, child brides of Jim Kleeman and Tom Doe, thought of this is not recorded.

We also saw a tape of Tim Bech receiving the “Human Condition Award” from the Heinz Foundation, which led to other accolades since our last reunion, including Marty Gordon’s Distinguished Service Award and leadership of the associations of the Medical Library and Vinny Londono’s role in Pfizer’s development of Viagra—functioning.

Our guest of honor is LEVON WATERS Jr.’s widow, Priscilla Norton, who with Howard Sweets is writing a biography of Milton Winternitz, former dean of the medical school and promoter of the Yale System. Vital memories were evoked of “Waters” and his pathology course, and for some—Bill Bannfield, Elly Wing, Bill and Molly Albin—Waters’s influence extended beyond our graduation.
1961
Our 60th reunion went very well. The program included a lot of fruits and vegetables included with the main course. Robert B. Y. Baker, Robert and Joyce Briggs, David and Judith Brook, Michael and Susan Burnham, John and Natalie Senn, David and Marco F. Griffith, Bernard D. Johnson, Larry Lyon, Christopher Lord, Vincent and Sally Marchesi, Anoush Mirandian, Rollo and Graziela Pellegrini, William and Melba Rodogno, Roy Kohn, Shuqin and Millennt Kudo, Robert Taub, Franklin and Lois Top, and Warren and Myis Widmann.

Levi Levy presented to Yale the fund that would become the Dr. Robert Levy Chair in Preventive Cardiology. This substantial gift had been raised from family, friends and supportive companies. Eight other classmates spent much time writing suggestions for a class seminar entitled “If You Had the Time to Go to Medical School Again. What Changes in the Curriculum Would You Recommend?” Their efforts culminated in a 32-page handout. Our alumni suggestions help to expand the horizons of the Education Policy Curriculum Committee (the ipec) of the medical school. The committee consists entirely of house officers, the four student representatives to the alumni council. As a class, we cannot be expected to be comprehensive, but our advice is quite relevant.

Vincent Marchesi hosted the class meeting at the Center for Molecular Medicine on Saturday. It was noted that the curriculum was providing much more of Yale that support for teaching, although, alas, someone has fallen behind. It was encouraging to see how well our graduates have become the leaders of medical societies on the Quimby Club, and at Sunday breakfast, Lois and Frank Top topped our list of suggestions that our contribution funds to reward excellence in teaching. Others pointed out that identifying a single best teacher of the year can be difficult and that a student survey may turn into a popularity contest. Vincent suggested that alumni arrange to take a medical school class to dinner with their classmate instead of the slides. Probably a good thing, he didn’t have a banner to be done at night.

Saturday evening the class dinner was held at an Italian restaurant in Little Italy in the shadow of the People’s Building. It turned out to be very nice. Myself, thirty sat together.

The early part of dinner, who should show up but Dean Oken accompanied by two keepers, ladies from the alumni office. It reminded me of my beloved president, also with a Yale connection, making the rounds of the ballrooms of Yale. The alumni of the class of ’66 (Lan, seatadn-xa), no shrinking, violets, offered opinions and observations. The dean was reminded that he was going to have to feed that real big bottle. And, he was doing the new graduates and the world any favor by sending the lonely out on graduation day. Starvation? No.

As I was slurping half-shell perfect steamed lobster followed. . . Did we live in the golden age, we would buy a few months today.

Tom H. Jackson 1971
The 50th reunion of the Class of 1971 was attended by 24 of our classmates: Drs. Bates, Cates, Cossian, Edward Foster, Gorden, Klein, Krieger, Lewis, Miller, Missache, Minnihan, Moggridge, Morgan, Patti, Perlman, Rand, Reichard, Rello, Stempfer, Travers, Tinsdale, Vaquers, Violina, Weihl, Woodhouse, and Zamarin. The class dinner was high.

Mary Alice Houghton replied, “Neither have you.”

Saturday evening there were impressive presentations on neuroscience, from remote testing to cellular to genetic level Geo-wiz computer graphics. I recall how because of some disease some dyspepsia, gus, and poor. As well, they look like they work pretty hard. When I mentioned some of some lads I had lost this past winter, he told me those were of heavy, strength-training. He looked for an annual lecture in her honor was discussed at a Mandel Hall in kitchen late at night.

Alice Ann Bernet Houghton and husband Bill (both ’54) are both still practicing psychiatry in Milwaukee. I understand psychic insight is little help in raising children, and traditional methodologies (sleep, calamar, Coca-Cola, et., how common—is that?) in are composed exclusively of the physician who does a little work on 2-1/2 letter-state abbreviations, e.g., pact = Pennsylvania (PA) + Connecticut (CT). An unanswered query is what can common medication can also be so composed. The answer will be given at the 50th reunion.

See you there.

David Uppman 1956
Practicing family—delaying ar-
lines, having a pretty good car, early on Wednesday, May 31, I headed east with CDs of late string quartets of Beethoven and a lengthy audio book to read. Thursday saw some last-minute details and the day fell into a popularity contest. We all agreed we were in that golden age. It was noted that we had fallen behind. How to encourage good teachers became the topic of discussion.

Earlier in the afternoon, Thursday. Walked a lot.

The class dinner was high where I was having a heart attack.

At night I accompanied by two keepers, during the class dinner I was’exhawking’ to the topic of teaching, although strong, has fallen behind. It would be rewarding to see how well our graduates have become the leaders of medical society.

The 30th reunion of the Class of 1956 is having cervical and renal problems. Mrs. Mirandian. Mrs. Mirandian, Mrs. Mirandian, Mrs. Mirandian, Mrs. Mirandian.

The class members briefly recited their career including the University of California at San Francisco, and the University of California at Denver.

I proclaimed,” I think it’s time that we have a little bit of a break from the routine for the new graduates and the world any favor by sending the lonely out on graduation day. Starvation? No.

As I was slurping half-shell perfect steamed lobster followed. . . Did we live in the golden age, we would buy a few months today.

Mimi Brown in medical oncology, from the University of California at Denver, and the University of Chicago. I understand psychic insight is little help in raising children, and traditional methodologies (sleep, calamar, Coca-Cola, et., how common—is that?) in are composed exclusively of the physician who does a little work on 2-1/2 letter-state abbreviations, e.g., pact = Pennsylvania (PA) + Connecticut (CT). An unanswered query is what can common medication can also be so composed. The answer will be given at the 50th reunion.

See you there.

David Uppman 1956
Outstanding 50th reunion, a trib-
ute to the vitality and youthfulness of our class! Delighted Friday night clubmate, Saturday lunch and fish-and-chips to celebrate, and dinner on Saturday night. At the last minute, the family and friends came from as far away as Buenos Aires (Richard) to California (Low) and Connecticut (Kessler and Marchesi). The class dinner was high.

Attending were Sarah Auch-
vicnch, M.D. (private practice psychiatry, New York); John Jefferson Oshin, M.D. (private practice dermatology, New York); Norm Kohn, M.D. (private practice neurology, San Diego); and Richard Kaye, M.D. (private practice endocrinology, Chicago); Joe Cates, M.D. (private practice cardiology, Westport, Conn.); and wife Karen (O.7). Also, Richard Low (CIO, FastMed Corp, Buenos Aires and Woodland Hills, Calif.) and wife Isabell; a MANDRAULUM (ophthalmology, New York); and Diane Oshin; Cindy Mann (private practice ophthalmology, Palo Alto, Calif.); Laurie Millicent (professor of laboratory and Molecular Biology, Yale); Richard Schotten-
feld (professor of psychiatry, Yale, and the new master of Downtown College); Peter Swanson (family practice, Shelton, Conn.); Charlie Swanison (associate professor of clinical psychology, University of Massachusetts); Bob Taylor (oncology, Milwaukee); Peter Ting, M.D. (private practice cardiology, New York); Maureen (Mann) Willie (private prac-
tice dermatology, New London, Conn.); Jon Mann (psychiatry, New York); Andrew Zimuckis (associate professor of medicine, Johns Hopkins) and husband Terry.

Classmates responding but unable to attend were: Richard S. Rivish, M.D. (physician-in-chief and chair of pediatrics, St. Joseph’s Children’s Hospital, Philadelphia, Pa.); Roger Bousha (assistant profes-
or of psychiatry, Harvard at Fall River, Mass.); P. Alan Cates, M.D. (private prac-
tice ob/gyn, Poway, Calif.); Joseph Ciaraturo (fish, New Haven); and the family of Bradford Terry.

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See you there.
Richard Kayne

The good news is that we had a
20th in 2006! I am hoping this letter will

Jeffrey Meyerhardt

Most of us seemed quite content

Diane 14, Stephen 12, and Gregory 10, all with great nicknames.

Lisa's father, Sandy Flam, and family;

Most of the classmates in attendance. For 2006, the most

We have two children—Steven, 11, and Jack, 9. We

for the 20th in 2006. I am hoping this letter will

Nutshell

He is also an ophthal-

dentified (internal medicine

So, we will have the 20th reunion class

knew and loved as director of the

The regular reunion class in 1986 was the 19th reunion class.

Dana Loo

Most of us seemed quite content

The weekend was a

The 20th reunion class had a

and his wife, Maria Almeida, with whose(...) who had been a chief

This year’s fifth reunion class had a

The 20th reunion class had a

and Jack, 9, with husband Craig Sterling and

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The most refreshing conclusions

Hopefully we will all have that

We have two boys and a girl (Isaac, Hannah, Jem, and Emily, 8). One of these people were in New Haven,

At Harkness, Mike had a great time at reunion.

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Robert Wood Johnson University Hospital in 1996. His clinical interests include pancreatic surgery, surgical oncology and endocrine surgery. He has long pursued research directed at elucidating the response of host cells, namely neutrophils, to neomolecular surfaces utilized in biomedical implants and devices. Greco, his wife, Irene Wagner, ’64, and their three children moved to Palo Alto, Calif., in August 2000.

NOTES

1960s

JOSEPH P. CUMING, M.D., ’64, reports that he is still in a solo pediatric practice after 31 years. Michael, received his M.D. from UConn and is in a pediatric residency in Virginia. Anne has put her Harvard law degree aside and is a pediatric resident in Vermont. I thoroughly enjoyed representing the medical school at the Tercentennial weekend.”

1970s

Ralph S. Greco, M.D., ’68, ’73, was appointed the Johnson & Johnson Distinguished Professor and chief of the Division of General Surgery at Stanford University School of Medicine, where he is also director of the General Surgery Training Program. After completing his surgical training at Yale, Greco spent two years in the U.S. Army Medical Corps in South Korea, and Fort Meade, Md., and then joined the faculty at the former Rut- gen Medical School. He became a full professor there in 1983, three years before the school changed its name to the Robert Wood Johnson Medical School. Greco was appointed chief of surgery at Orange County Projects. He then continued within the ccc to become the team leader of the Acute Care Team within the National Center for Injury Prevention and Control (NIPC). Since 1999, he has served as the acting director of the NIPC’s Division of Acute Care, Rehabilitation Research, and Disability Prevention, which provides national leadership in preventing and minimizing the impact of nonoccupational injuries. His goal is to engineer a shift in the way medicine is taught and researched toward a population orientation that includes prevention and complements the clinical approach of treating one patient at a time.

1980s

INGI S. CUSHMAN, M.D., ’76, was elected president of the American Academy of Physician Assistants. She has held a variety of other positions within the organization in the past. She is a senior physician assistant with Harvard-Van- guard Medical Associates, a private practice group providing primary care in the United States, which he attributed to racial bias. He spoke about the history of this phenomenon and challenged his audience to try to eliminate health care disparities for society’s well-being.

In a biographical sketch for the Centers for Disease Control and Prevention (CDC), Daniel A. Pollack, M.D., ’79, described a change in his career as follows: “In my work as an emergency physi- cian, I saw the same injury types again and again and again. As a result, I thought it would be important to learn injury demographics and causes, and to find ways to prevent injuries, instead of contin- uously treating them and trying to limit their effects.” This connection led him from a position as an intensiv- e care practitioner who oversaw patients who were critically ill to a role at a hospital where he could focus on the prevention of injury and disease. He also recognized that the prevention of injury and disease was a global issue, and he became involved in international efforts to address this problem.

Michael Simmons, M.D., M.B., ’89, ’B.S., has been appointed the Arna Gundlach Huber Professor of Medicine and chief of the Section of Cardiology at Dartmouth Medical School. He moved to Dartmouth from Harvard Medical School, where he was an associate professor of medicine and director of the Angiogenesis Research Center at Beth Israel Deaconess Medical Center. Simmons transported his entire lab northward, including almost 20 researchers and $2 mil- lion a year in funding from the National Institutes of Health, the American Heart Association and industry sources. His research in angiogenesis focuses on the use of a growth factor called PEG to stimulate blood vessel growth.

Send faculty news to: Claire Beisinger, Yale divinity, P.O. Box 3612, New Haven, CT 06519-0612, or via e-mail to claire.beisinger@yale.edu.
Donald J. Cohen, M.D., ’66, director of the Yale Child Study Center, founding director of Child Psychiatry, Pediatrics and Psychology, died October 9 at a year-long illness. He was 64.

Cohen graduated from the School of Medicine in 1966, joined the Yale faculty in 1970, and in 1978 became director of the Yale Child Study Center. Under his leadership the Child Study Center became the largest and most internationally recognized for its multidisciplinary programs of clinical and basic research, professional education, clinical services and advocacy for children and families. Cohen’s clinical and research activities focused on developmental psychopathology of the serious neuropsychiatric disorders of childhood, including autism, pervasive developmental disorders and tic disorders such as Tourette’s syndrome. He led the study in the impact of violence on children and families created a worldwide network of collaborators.

Cohen published more than 400 articles, chapters and books. He was a trustee of the International Association of Child and Adolescent Psychiatry and Allied Professions, chair of the publications committee and vice president of the Association of Yale University Press, co-chair of the Child Health and Development Institute, and the second president of the Tekfon Azur Foundation in Italy and chair of the international Advisory Committee of the Schneider Children’s Hospital of Israel.

He was a member of the Institute of Medicine of the National Academy of Sciences and a training and supervising psychoanalyst at the Western New England Institute of Psychoanalysis. He received numerous awards, including an honorary degree in 1997 from Bar-Ilan University in Israel for his contributions to children’s psychiatry and the mentorship of young professionals in Israel, a Special Presidential Citation from the American Psychiatric Association and a lifetime of Research in Autism Award from the National Alliance for Research on Schizophrenia and Depression.

Kenneth Colby, M.D., ’74, a psychiatrist and a Pioneer in artificial intelligence and computerized therapy, died on April 9 at his home in Walnut Creek, Calif. He was 81.

In the early 1970s, Colby led a team that developed the software program Parry, which was designed to imitate the paranoia of a schizophrenic. In text input, psychiatrists were unable to distinguish Parry’s responses from those of real paranoia. Parry was only the program to pass the “turing test,” meaning that it could successfully impersonate a person in a typed conversation.

In 1989, Colby and his son, Peter, founded Alibu Artificial Intelligence Works to develop therapeutic software. One program they designed was called “Overcoming Deceit,” and it combined a text-based artificial intelligence and techniques and a free association component. The program was used by the Department of Veterans Affairs, the Navy and Kaiser Perma-

nente, among others, to teach people with mental illness who do not seek professional help.

Colby was born in Watertown, Conn., and graduated from both Yale College and the School of Medicine. He practiced psychiatry for 30 years, and then was a professor of computer science at Stanford University, where he created Parry at the university’s Artificial Intelligence Laboratory. He moved to crica in 1975 to teach in the psychology and biochemistry sciences department. He retired from aca-

demia in 1989, when he started Alibu Artificial Intelligence Works to develop therapeutic software. One program they designed was called “Overcoming Deceit,” and it combined a text-based artificial intelligence and techniques and a free association component. The program was used by the Department of Veterans Affairs, the Navy and Kaiser Perma-

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Robert I. Hinkley, M.D., ’44, a general practitioner in Groveton, N.H., died on April 13 at the Morn-

ington Nursing Home after a brief illness. He was 81.

Born in Lancaster, N.H., Hinkley graduated from Bowdoin College in Maine and then received his M.D. from Yale. He did an internship at Worcester City Hospital in Massa-

chusetts and then served two years in the Army as a post surgeon at the Ogden Ord-

nance Depot. After returning to his practice in 1923, he attained the rank of captain.

After returning on the military, he settled in Groveton and re-

mained there for the rest of his life. He started a general practice in 1922 and was on the staff of Weeks Hospital until his retirement in 1966. He founded the first ambu-

lance and medical care unit at Weeks. He was also president of the staff for two years and served on the hospital’s Board of Trustees.

Hinkley was widely involved in local and state societies and founded the Coos County Medical Society. He was also elected a charter fel-

low of the Academy of Family Physicians in 1975. He was appointed to the New Hampshire Milk Sanitation Board by the gover-

nor for many years, he was the Groveton and Stark health officer, and he also served on the Groveton school board for nine years. He was a trustee of the New Educational Foundation and served as president of the Groveton Foundation.

Additionally he was a senior man-

ter in duplicate bridge and shot golf rounds in the 70s in each of seven decades.

Ed, Leonard Kessler, M.D., ’49, a clinical professor of surgery at the University of Connecticut School of Medicine and a distinguished thora-

acic surgeon, died on May 2 in Boston from leukaemia. He was 82.

Kessler lived in Sherman, Conn., where he would return to resid-

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Donald D. Waido, M.D., M.P.H., ’51, died January 15 at Med-Cen-

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Donald W. Dewald, M.D., M.P.H., ’44, a professor emeritus of Family Physicians in 1975. He was appointed to the New Hampshire Milk Sanitation Board by the gover-

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ter in duplicate bridge and shot golf rounds in the 70s in each of seven decades.
Upon arriving in Ganta [Ganta Methodist Mission Hospital in the hills of eastern Liberia], I soon discovered that tropical medicine would be considered a general practice by American standards. For example, on any given morning the first five people in the clinic line might include a child with amoebic dysentery, a man suffering for a long time with onchocerciasis, a boy whose blood smear for *P. falciparum* is 6 plus positive, a pregnant mother of eight who complains of back pain, and an old man whose scrotum extends almost to his knees. Later in the morning things might become somewhat more hectic. While you are examining a child with chickenpox, you send a man who has obviously broken his femur to the emergency room and hope that the woman who has just been taken into the examining room doesn’t have an ectopic pregnancy as suspected. It’s hectic because you can’t send the man with the broken femur to X-ray. Instead you do the alternative: that is, you roll out the old U.S. Army field unit and trust that there’ll be enough power to take a respectable film. You can’t send the pregnant woman to surgery for, unlike as it might seem, you are surgeon! In many ways one might consider such an experience a rotating internship. But instead of rotating every two months, you rotate with each new patient.”

“Growth in medicine has meant growth in the Library... A visit to the computer-search office gathers in a few minutes a volume of citations that would have taken days of hand searching. The computer terminal has available to it Medline, the online database equivalent to the last three years of Index Medicus... Technology now being developed holds even greater promise for libraries and library users. The National Library of Medicine, which developed Medline in the sixties, is working on a videodisk system that could fundamentally alter the concept of publishing. Electronic ‘publications’ of journals, whether through videodisks or some other method, would eliminate paper copies. Readers could use computerized bibliographic searching to find references, then scan the articles on a computer terminal screen... Eventually, perhaps as soon as the end of this century, books too would be published in electronic form. While older books and journals would survive—and need to be stored—current publications would take up far less room. And their content would be available to computerized searching, freeing researchers from mechanical tasks to concentrate on the information itself.”

**ALUMNI QUESTIONNAIRES TO BE MAILED SOON**

The School of Medicine will publish an updated alumni directory in the autumn of 2002, providing contact and professional information for more than 11,000 graduates of the School of Medicine and its training programs. The directory will list alumni alphabetically and by program, class year, geographic location and area of medical specialty. The last medical school alumni directory was published in 1997.

The Bernard C. Harris Publishing Co. will be mailing a questionnaire to each alumnus and alumna at the address below so we can make sure you receive a directory questionnaire.

Association of Yale Alumni in Medicine
Spinelli Office of Alumni Affairs
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100 Church St. South
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New Haven, CT 06525
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