

Yale Medicine

Center to support
teaching

4

Nanoparticle aids
gene therapy

6

Scholars and New
Haven

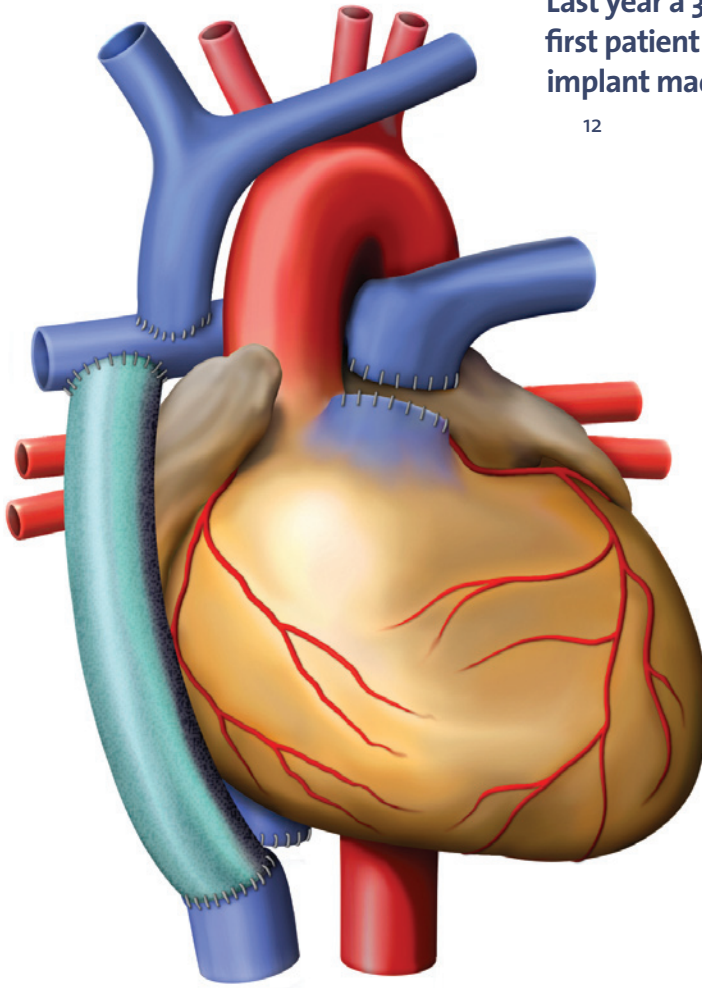
18

spring 2012

Tissue from the lab mends a broken heart

Last year a 3-year-old Bridgeport girl became the first patient in the United States to receive an implant made of bioengineered tissue.

12



ON THE COVER Using a bioengineered graft made with cells from her own bone marrow, Yale surgeons rearranged blood flow in the heart of a girl born with only one functioning ventricle.

Illustration by Steven Hall

THIS PAGE Angela Irizarry played in her bedroom with her brother, Alexander. Last year she became the first patient in the United States to receive a bioengineered heart vessel.

Photo by John Curtis



SPRING 2012

CONTENTS

- 2 Letters
- 4 Chronicle
- 8 Books & Ideas
- 10 Capsule

- 12 **Tissue from the lab mends a broken heart**
Last year a 3-year-old Bridgeport girl became the first patient in the United States to receive an implant made of bioengineered tissue.
By John Curtis

- 18 **Scholars work toward healthy communities**
Yale's Robert Wood Johnson Clinical Scholars make a point of engaging the community in their research and making the world a healthier place.
By Jennifer Kaylin

- 24 Faculty
- 26 Students
- 28 Alumni
- 32 In Memoriam
- 33 End Note

On the Web yalemedicine.yale.edu

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



HOW TO REACH US

Yale Medicine welcomes news and commentary. Please send letters (350 words or fewer) and news items to *Yale Medicine*, 1 Church Street, Suite 300, New Haven, CT 06510, or via e-mail to ymm@yale.edu, and include a telephone number. Submissions may be edited for length, style, and content.

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On physician-scientists

Congratulations to Colleen Shaddox for a very interesting and timely article in the Autumn 2011 edition ["Is the physician-scientist an endangered species?"]. I published an article in *Yale Medicine: Alumni Bulletin of the School of Medicine* in the spring of 1972, titled "Sicklelema: The Doctor Bird Visits a Political Arena." As a student advocate I helped to form the Sicklelema Cell Committee of South Central Connecticut between the community of New Haven and the School of Medicine. Then I graduated from the School of Medicine in 1973 and have been practicing internal medicine ever since. I'm proud to have left a contribution to the community. It's important to be able to think outside the box if physicians are to contribute to science or their local communities.

*Robert E. Galloway, M.D. '73,
M.P.H., M.B.A.
Houston, Texas*

Concern is expressed in the Autumn 2011 issue about the future of the physician-scientist. Clearly the benefits that medical research has bestowed upon humanity are remarkable, thanks to the efforts and perseverance of research physicians' inquisitiveness and their relentless pursuit of answers. But do medical researchers necessarily have to be M.D./PH.D.s?

Almost 100 years ago, Sir William Osler, a respected clinician, author of a widely read medical textbook, and one of the founders of the Johns Hopkins University School of Medicine, believed that medical researchers should confine their labors to research institutes and that physicians should be trained by community-based physicians in private practice. He thought that the separation would be beneficial because it would lead to the training of more practical-minded physicians. Osler also believed that

physicians living in the community would bring a practical and humanistic viewpoint to the medical wards that research scientists who are focused on the purely scientific components of illness are incapable of.

But Abraham Flexner—who was an educator, not a physician—held the contrary position. He believed that physician-scientists should be trained in the university and that full-time professors of medicine should train physicians. With the backing of the Carnegie Foundation and the Rockefeller Foundation, Flexner prevailed. The orientation of American medicine has been research-based ever since. Some believe that the lack of primary care physicians is partly due to the disproportionate attention to medical research compared to primary care. The effects of Flexner's influence on medical education are now being questioned by some medical educators.

The point is that medical research is absolutely necessary for medicine to advance. How much research and what kind, however, are questions that need to be addressed. Osler's idea of separating physician-clinicians and physician-scientists, as heretical as it may sound today, may have merit. Perhaps fewer M.D./PH.D.s will not have a generally negative effect on medical progress. Maybe more PH.D.s working in research institutes and collaborating with physician-clinicians is a model that should be studied.

It would lessen the focus on medical research and place more emphasis on the training of primary care physicians. Is that necessarily a bad thing?

*Edward J. Volpintesta, M.D.
Bethel, Conn.*

In "Is the physician-scientist an endangered species?," Colleen Shaddox outlines the School of Medicine's noble efforts to encourage young people to become the medical researchers of the future. The major threat to the developing physician who undertakes basic science research is that this species is a financial liability in most academic departments.

When faculty members are told by their chairs that they must "cover their salary," they encounter a conflict. On the one hand, a physician-scientist typically needs two NIH RO1 grants to pay a significant portion of salary and cover the expenses of doing research. And it is hard to see how one could successfully run such a lab without at least 90 percent effort. To cover the remainder of his or her salary typically means generating income through clinical work. When one considers the costs of seeing patients (malpractice, room rental, administrative support, etc.), however, the break-even time point is typically about 40 percent effort. In the current academic department business model, there simply is not enough time to be an effective basic science researcher and see enough patients to cover the remaining salary costs. The exception to this situation occurs in wealthy departments—either surgical departments or those with profit-generating procedures. To the extent that departments must keep their financial house in order, there is a major disincentive to carry physicians who undertake basic science research. Departments and medical schools must find intrinsic merit in physician-scientist faculty members and support them accordingly, or the physician-scientist will go the way of the dodo bird.

*Robert G. Kalb, M.D., Hs '87, FW '90
Professor, Neurology
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Yale Medicine goes viral

As one who came of age professionally in the era of print and attended a high school that kept academic records on punch cards churned out by an off-site computer as big as a warehouse, I'm still amazed by the possibilities of the digital age. Two e-mail messages that arrived on the morning of January 30 reminded me of the increasing power of social media.

Debby Jagielow, director of alumni affairs for the medical school, wrote to say that our Winter 2012 cover story about Yale medical students who had launched Nyaya, a clinic in a remote corner of Nepal, was receiving many, many "likes" on Facebook.

The next message came from Pete Farley, managing editor of our sister publication, *Medicine@Yale*. On January 29, a *New York Times* columnist, Nicholas Kristof, and Peter Singer, the Ira W. DeCamp Professor of Bioethics at Princeton, had tweeted the article by freelancer Stephanie Soucheray-Grell. "Great piece on Yale med students who started a new style of NGO, saving lives in one of the poorest regions of Nepal," Singer tweeted.

That same day Facebook and Twitter drove 1,050 viewers to our site. Our website usually draws about 900 visitors *per month*.

Is there a lesson here? I like to think that this surge in Web traffic resulted from a series of fortunate events. We had a compelling story about a new approach to providing health care in the developing world—the story struck a chord with two well-known people who speak out on behalf of the marginalized and forgotten. The most gratifying news, however, came from Nyaya's founders, who said that *Yale Medicine* has helped put their project in the public eye, and that in turn will help them to fulfill their mission of saving lives in Nepal.

It was also gratifying to learn in January that an article in our Spring 2011 issue, "The High Cost of a Medical Education," by freelance writer Sonya Collins, had won an Honorable Mention award from the Association of American Medical Colleges' Group on Institutional Advancement.

John Curtis
Editor

SECOND OPINION BY SIDNEY HARRIS



yale medicine

*Alumni Bulletin of the
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New center to support novel teaching methods

Its goal is to enhance the learning experience for students and elevate the status of teaching.

A new center opened in February in a handful of rooms on the second floor of Harkness Building A. The Teaching and Learning Center was created to address two issues at the heart of the School of Medicine's effort to review its medical curriculum and bring it in line with the practice of medicine in the 21st century. One issue is the place of new educational technology; the

other is the long-standing tendency in academic medicine to reward research and clinical care over teaching.

"We want to enhance the learning experience for our students and elevate the status of teaching by putting in place the kind of support and expertise our faculty can use to develop new teaching methods," said Richard Belitsky, M.D., deputy dean for education and the Harold W. Jockers Associate Professor of Medical Education, who is developing and overseeing the center.

The center is a direct result of the School's Strategic Plan for Medical Education. A planning committee report issued in 2010 was unambiguous in determining that teaching should be a top priority. "The need to better recognize, support, and reward teachers and educators has emerged as a central theme and clear recommendation of this strategic planning process, just as it had in each of the four prior strategic planning efforts," the report stated.



The Teaching and Learning Center (TLC) has a conference room, offices, and computers. It will offer programs, seminars, services, training, and consultation in three areas: educator development, assessment, and technology. The center will provide help with assessment methodology and interpretation of evaluation data in student learning, curriculum effectiveness, and quality of teaching.

Belitsky sees the TLC as an important step toward “fulfilling the promise of the strategic plan.” To be leaders in medical education, he said, “we need to think carefully about the learning strategies of our students. They are highly influenced by new technologies, so we need to make sure our faculty is facile with them, too.” One example is the school’s recent decision to give iPads to all students. The electronic tablets enable students to download the entire curriculum and will be used increasingly by professors as a teaching tool to engage students in new ways.

The center will have four associate directors. Janet P. Hafler, M.ED., ED.D., will serve as the associate director for educator development; Frederick D. Haeseler, M.D., FW ’76, is the associate director of learning and technology; and Gary B. Leydon will be the associate director for technology services. A national search for an associate director for learning and assessment is under way.

Gary Leydon, Rick Haeseler, Janet Hafler, and Richard Belitsky lead the new Teaching and Learning Center, which opened in February. The center’s goals are to enhance students’ learning experience and recognize excellence in teaching.

Haeseler says he views his new role, which Belitsky describes as “marrying technology and pedagogy,” as an outgrowth of his work as director of the Standardized Patient Program and as founder and director of the Primary Care Clerkship. Haeseler expects that the strategic plan will inspire the integration of a variety of pedagogies into the medical school’s new curriculum. The TLC could help facilitate this process by adapting such innovative technologies as electronic medical records, cloud computing, handheld devices, asynchronous learning, distance learning, and low- and high-fidelity simulation. Haeseler also brings to the TLC a team of seasoned standardized patients, who participate in a variety of teaching venues throughout the first three years of the medical school curriculum. He expects that the standardized patient program, with its many illness scenarios and its emphasis on patient-centered communication, will continue to evolve to meet the needs of faculty and students in achieving the school’s overarching goals.

Still, with all the focus on new technologies, new pedagogies, and new ways of teaching and learning, Belitsky wants to make sure the old ways aren’t abandoned. He says he’ll be watching closely to make sure that whatever is introduced is “consistent with the Yale system and the learning environment we all cherish.”

—Jennifer Kaylin

et cetera ...

YSM, PHARMA TO COLLABORATE

Yale and the Johnson & Johnson Corporate Office of Science & Technology (COSAT) have signed an agreement to fund activities at the Yale Small Molecule Discovery Center (YSMDC). The YSMDC helps validate potential biological targets for new drugs and molecules.

“This sponsorship of the YSMDC comes at a time when academic and pharmaceutical scientists are increasingly looking to collaborate in order to help fill the pharmaceutical pipeline with the medicines of tomorrow,” said Thomas E. Shrader, PH.D. ’90, director of strategic corporate partnerships in Yale’s Office of Cooperative Research.

“This collaboration will allow Yale scientists to focus on the parts of this pathway that we do best—identifying novel disease targets, while getting COSAT’s expertise in the areas where Yale, and most universities, have limited experience,” said Michael S. Kinch, PH.D., managing director of the YSMDC.

—John Curtis

WHEN YOU GOTTA GO

A strong need to urinate impairs cognitive faculties as much as fatigue or an alcohol buzz, according to researchers at Yale, Brown, the University of Melbourne, and the Australian company CogState.

“Giving people lots of water and making them take tests while squirming in discomfort may seem a bit quirky, but the research helps us evaluate the methods used to measure cognitive change,” said Robert H. Pietrzak, M.P.H., PH.D., assistant professor of psychiatry at the School of Medicine. The research garnered the 2011 Ig Nobel Prize in Medicine from the humor magazine *Annals of Improbable Research*.

For the study, published in January 2011 in *Neurourology and Urodynamics*, healthy adults drank 250 milliliters of water every 15 minutes and took cognitive function tests every hour. The resulting impairment in attention and working memory matched that observed in people who have a 0.05 percent blood alcohol concentration or have remained awake for 24 hours. The subjects’ cognitive functions “returned to normal almost immediately after voiding.”

—J.C.

Gene therapy takes a step forward with a synthetic nanoparticle

The particles injected into the tail of a lab mouse course through the animal's veins, eluding immune surveillance as they make a stealth run toward the tiny tumor growing on its flank. When the particles hit the tumor, the raid begins in earnest. The particles slip through the outer cellular membranes and into the rogue cells. The genes packaged within the particles shed their protective polymer veil and hijack the cellular machinery. From there, the covert DNA instructs the cells to produce apoptosis-inducing proteins, which trigger cell suicide and ultimately sabotage tumor growth.

This gene therapy success story, published online in December in the journal *Nature Materials*, marks a paradigm shift in the method for delivering therapeutic genes to diseased cells. At the root of this triumph is a biodegradable nanoparticle created by Yale biomedical engineers that upends previous dogma.

As W. Mark Saltzman, PH.D., the Goizueta Foundation Professor of Biomedical Engineering, co-principal investigator with associate research scientist Jiangbing Zhou, PH.D., and research scientist Zhaozhong Jiang, PH.D., explains it, researchers previously used viruses to ferry genetic material into animal cells. These foreign particles, however, appeared as red flags to the host's immune system, resulting in their swift demise. Earlier engineers replaced the viral vectors with synthetic nanoparticles, which they believed needed a high positive charge to glom onto negatively charged DNA and condense it into a neat little package for intracellular delivery. These charged nanoparticles did the job, but their excess positive charge also destabilized cell membranes, causing considerable toxicity.

The Yale researchers hypothesized that replacing some of the excess



MICHAEL MARSLAND

positive charge with hydrophobic regions might reduce the toxicity of the polymers yet still allow for condensation of DNA. They developed a controlled system of polymer synthesis that allows them to tune the polymer constituents, tweaking where necessary to find the right balance between positively charged and water-insoluble units.

Among the 20 polymers that the Yale team constructed, one exhibits the ideal mix of sticky positive charges and hydrophobic regions. When mixed with DNA, the polymer condenses to create nanoscale spheres that resemble minuscule water droplets on a pane of glass. The compacted DNA tucked within the nooks and crannies of the polymer blobs is protected from enzymatic assault when circulating in the body. Equally important, the nanoparticles pose no harm to the animal host.

When tested in vitro, the nanoparticles delivered genes to target cells with 50- to 170-fold-greater efficiency than commercially available gene therapy

vectors. Furthermore, tumor-bearing mice regularly dosed with the apoptosis-inducing gene therapy showed no toxicity during the entire course of treatment, and their tumors grew to only a fraction of the size of those in control mice. Closer inspection of the tumor tissue revealed that the suicide gene dramatically promoted the death of tumor cells.

Saltzman envisions someday using the new polymer delivery system in humans to enable gene therapy for several diseases, including cystic fibrosis, Huntington disease, and cancer, particularly brain tumors—a devastating disease that he says demands heroic efforts. “We’ve been developing techniques for introducing particles like these directly into the brain to treat malignant brain tumors for some years. Our hope is that these polymers give us another tool—a very safe tool—that we can use in that arena,” Saltzman says.

—Kara Nyberg

Grant funds study of rare disorders linked to single mutant genes

While some diseases stem from a web of influences including environment, lifestyle choices, and genetic luck, others result from a single mutant gene. While the inheritance patterns of these so-called Mendelian disorders are straightforward, finding the errant genes is not.

More than 6,000 rare Mendelian disorders have been identified in the United States. Collectively, they afflict more than 25 million people, but each affects fewer than 200,000 people. The fewer patients who have a disease, the harder it is to study, because both funding and genetic samples are limited—yet discerning their genetic causes may lead to treatments and yield broader insights into human biology.

“There are roughly 22,000 genes in the human genome,” said Richard P. Lifton, M.D., Ph.D., chair and Sterling Professor of Genetics and a principal investigator of a new grant from the National Institutes of Health. “Right now we know what diseases result when about 3,000 of those are mutated. We know almost nothing about what happens when the remaining ones are mutated.”

The new four-year \$11.2 million grant has established the Yale Center for Mendelian Genomics, to be located on the West Campus. The grant, announced in December, will fund two other centers devoted to Mendelian diseases—one at the University of Washington in Seattle and one operated jointly by Baylor College of Medicine in Houston and the Johns Hopkins University in Baltimore.

At Yale, principal investigators include Murat Günel, M.D., HS '98, the Nixdorff-German Professor of Neurosurgery and professor of genetics and of neurobiology; Shrikant Mane, Ph.D., senior research scientist in genetics; and Mark B. Gerstein, Ph.D., the Albert L. Williams Professor of Biomedical Informatics and

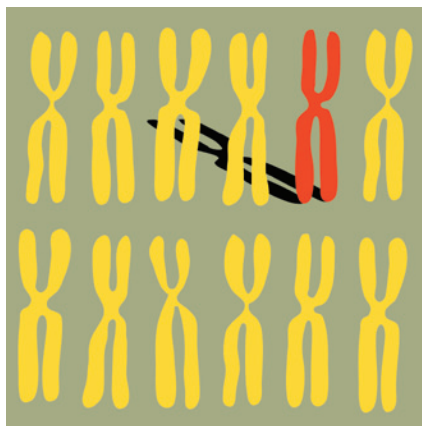
co-director of the Yale Computational Biology and Bioinformatics Program.

Underlying the new project is exome sequencing, a gene sequencing method that targets those parts of the genome that encode proteins. Many inherited diseases are thought to be due to mutations in the exome. “The new sequencing technologies enable us to pinpoint disease-causing genes even with only a few affected subjects. This has really opened up the field,” said Lifton, a Howard Hughes Medical Institute investigator.

The new center hopes to identify patients with these mutations and learn the consequences of each genetic deviation. “Identifying the specific genetic causes of these diseases will be useful diagnostically; the therapeutic possibilities will only be revealed when we can link mutations to disease traits,” said Lifton.

The Yale team also expects to learn some lessons in basic biology. The link between each gene mutation and disease can teach scientists a great deal about what happens when those same genes function normally, Lifton said. “It really tells us how each gene works in the context of the human body. And this tells us a great deal about how entire pathways work, which is very important to future drug development.”

—Sarah P.C. Williams



OTTO STEININGER

et cetera ...

ABUSE, NEGLECT, AND GRAY MATTER

Emotional abuse and physical neglect lead to less gray matter in adolescent brains, according to a School of Medicine study published in December in the *Archives of Pediatrics and Adolescent Medicine*.

The brain areas affected may differ in boys and girls, may depend on whether the youngsters were exposed to abuse or neglect, and may be linked to whether the neglect was physical or emotional. The study of 42 adolescents showed reduction in gray matter in youths who reported abuse or neglect, even though the youths had not been diagnosed with a psychiatric disorder.

“This could help to explain their trouble with school performance, or increase their vulnerability to depression and behavioral difficulties,” said senior author Hilary P. Blumberg, M.D., associate professor of psychiatry and of diagnostic radiology and in the Child Study Center. More research is needed in order to develop improved interventions to help the youths who have been exposed, Blumberg said.

—John Curtis

ORPHANS NEED MORE TLC

Orphans may require more TLC than children reared by their biological parents, according to a study by Yale scientists published online in November in *Development and Psychopathology*.

Oksana Y. Naumova, Ph.D., and colleagues compared whole-genome methylation profiles based on blood samples from 14 7- to 10-year-olds raised in Russian orphanages and from 14 children growing up in typical families. Orphans showed changes in the genetic regulation of the systems controlling immune response and intercellular interactions—including mechanisms important in the development and functioning of the brain.

The stress of separation, the study found, affects the long-term programming of genome function. “Parenting adopted children might require much nurturing care to correct these biological effects,” said senior author Elena L. Grigorenko, Ph.D. '96, the Emily Fraser Beede Associate Professor in the Child Study Center and associate professor of psychology and of epidemiology (chronic diseases).

—J.C.

A physician's obsession

How a 19th-century doctor faced the demands of career and ambition.

William Beaumont, M.D., “the father of gastric physiology,” achieved fame in a less complicated time. To further his understanding of digestion, he began studying a fur trapper left with a permanent hole in his stomach following a shotgun accident in 1822. Born in Lebanon, Conn., Beaumont had skipped medical school, apprenticed to a Vermont doctor, then enlisted as a surgeon's mate in the War of 1812.

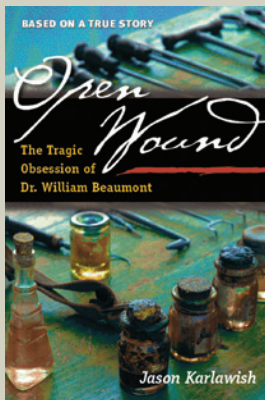
Those were simpler times.

Or were they? In his novelized account of Beaumont's life, Jason Karlawish, M.D., professor of medicine and medical ethics at the University of Pennsylvania, conveys the difficulties confronting a farmer's son who sought not only to make a name in medical research but to earn a handsome income in a location pleasing to his wife. Karlawish suggests that 19th-century pressures on physicians resemble those of the 21st: competing with better-credentialed colleagues; working for unsympathetic

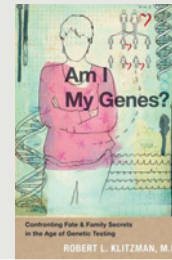
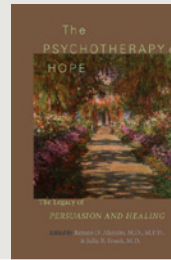
bosses; negotiating with a recalcitrant study subject; and balancing between family and career.

Beaumont did achieve recognition—faculty at the School of Medicine named a club, a lecture series, and a room after him in 1920. Speaking in the Beaumont Room in December, Karlawish said that Beaumont's desire to understand the digestive system spurred him to virtually enslave the injured fur trapper. And that, Karlawish said, reminded him of the tragedy of teenager Jesse Gelsinger, who died in a 1999 gene therapy experiment. “Those research pressures,” said Karlawish, “can make you make decisions that you might not otherwise make.”

—Cathy Shufro



Open Wound: The Tragic Obsession of Dr. William Beaumont



The Psychotherapy of Hope: The Legacy of *Persuasion and Healing* edited by Renato D. Alarcón, M.D., M.P.H.; and Julia B. Frank, M.D. '77, HS '81, FW '82 (Johns Hopkins University Press) Inspired by the work of Jerome D. Frank and his book *Persuasion and Healing*, this volume of essays broadly assesses the current state of research and practice in psychotherapy. Challenging the claims made for the superiority of cognitive-behavioral, psychodynamic, and other varieties of therapy, the authors—Frank's daughter and one of his former students—examine the values and limitations of competing approaches to diagnosis and treatment.

Am I My Genes? Confronting Fate & Family Secrets in the Age of Genetic Testing

by Robert L. Klitzman, M.D. '85 (Oxford University Press) Although genetic testing has improved the diagnosis and treatment of such diseases as Huntington, cystic fibrosis, and Alzheimer, it leads to difficult decisions for people who fear being tested and question what to do with the results. The author interviewed 64 people who face these dilemmas and describes how they have dealt with the implications of genetic findings for their own lives and those of their family members.

Hematology: A Pathophysiologic Approach

by S. David Hudnall, M.D., HS '82, professor of pathology and of laboratory medicine (Mosby) This text, part of the Mosby Physiology Monograph Series, offers explanations of hemato- poiesis, immunology, hemostasis, hemoglobinopathy, metabolic

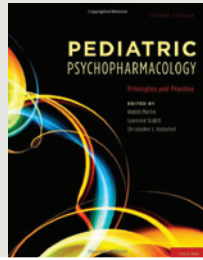
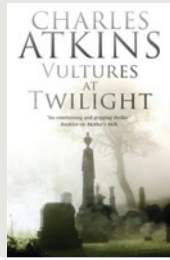
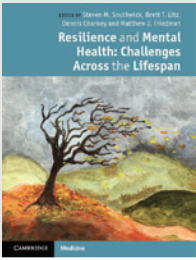
disorders, genetics, and neoplasia by using an integrated problem-based approach to learning. The author shows how hematologic disorders are evaluated through blood counting, histopathology, immunohistochemistry, cytogenetics, and coagulation testing. An online version is also available.

Desmoid Tumors

edited by Charisse Litchman, M.D. '88, HS '89 (Springer) This text, the first publication devoted entirely to desmoid tumors (DT), discusses this rare fibroblastic proliferative disease, which has an incidence of 2 to 4 new cases per million people per year. Clinical presentations, imaging guidelines, and treatment paradigms are highlighted, along with a discussion of the unique issues in treating children with DT. The book also describes emerging research techniques and the role of advocacy groups in supporting research and promoting awareness of such rare diseases as DT.

Resilience and Mental Health: Challenges Across the Lifespan

edited by Steven M. Southwick, M.D., HS '85, Glenn H. Greenberg Professor of Psychiatry, Post-Traumatic Stress Disorder, and Resilience; Brett T. Litz, PH.D.; Dennis Charney, M.D., HS '81; and Matthew J. Friedman, PH.D., M.D. (Cambridge University Press) This book brings together experts whose research has focused on adaptive responses to stress, which are less well understood than stress-related disorders. Each of the book's five sections examines relevant concepts, ranging from factors that contribute to and promote resilience to specific applications and contexts of resilience, as



well as interventions to enhance healthy adaptation to stress.

Vultures at Twilight

by Charles Atkins, M.D., lecturer in psychiatry (Severn House) Lil and Ada, longtime friends and neighbors in a Connecticut town, prove to be unlikely heroines when a severed finger shows up at the Friday night antiques auction, and they have to wonder: Where's the rest of the body? That question leads to the revelation of small-town secrets and the unraveling of a mystery that shows that all is not well in a town famed for its postcard-perfect New England charm.

Prenatal Diagnosis: Cases & Clinical Challenges

by Miriam S. DiMaio, M.S.W., senior genetic counselor; Joyce E. Fox, M.D., FW '86; and Maurice J. Mahoney, M.D., J.D., FW '70, professor of genetics, of obstetrics, gynecology, and reproductive sciences, and of pediatrics. (Wiley-Blackwell) This book is based on the authors' decades of experience during an era of rapid development in *in utero* diagnosis. The authors use real cases to portray diagnostic problems as a route to underlying biology, available testing options, and results that may be obtained. The authors discuss the challenges of management, interpretation, and counseling by emphasizing three types of clinical problems: chromosomal abnormalities; Mendelian disorders; and fetal structural abnormalities.

The Practice of Perioperative Transesophageal Echocardiography: Essential Cases

edited by Albert C. Perrino Jr., M.D., HS '87, FW '88, professor of

anesthesiology; Scott T. Reeves, M.D., M.B.A.; and Kathryn Glas, M.D. (Lippincott Williams & Wilkins) This text provides more than 100 teaching cases, presented in a question-and-answer, self-test format. The cases cover clinical challenges faced by perioperative echocardiographers, including disorders of the aorta, left ventricle, and right ventricle; valvular heart disease; congenital heart lesions; catheter and device placement; and unsuspected masses and thrombi. A companion website contains the fully searchable text plus echocardiographic video clips for each case.

Pediatric Psychopharmacology, 2nd ed.

edited by Andrés Martín, M.D., M.P.H. '02, Riva Ariella Ritvo Professor in the Child Study Center and professor of psychiatry; Lawrence Scahill, M.S.N. '89, M.P.H. '89, PH.D. '97, professor of nursing and child psychiatry; and Christopher J. Kratochvil, M.D. (Oxford University Press) The editors have streamlined the flow of information to reflect the accumulation of scientific data since the first edition. The overall structure of the book remains the same, with major sections on underlying biology, somatic interventions, assessment and treatment, and special considerations.

The descriptions above are based on information from the publishers.

SEND NOTICES OF NEW BOOKS TO Cheryl Violante, Yale Medicine, 1 Church Street, Suite 300, New Haven, CT 06510, or via e-mail to cheryl.violante@yale.edu



FRANCESCA DOMINICI

Summer heat deadlier

Research models that estimate how many people might die in urban heat waves will help government agencies better respond to them, said a biostatistician who predicts that air pollution will make summers in the United States deadlier by the end of the century. The research is also an argument for stricter regulation of pollutants, according to Francesca Dominici, PH.D., M.P.H., associate dean for information technology at the Harvard School of Public Health. Dominici was a guest lecturer at a School of Forestry and Environmental Studies seminar in January.

The most severe cardiovascular and respiratory effects stem from elemental carbon and organic carbon matter—pollutants that are one-twentieth the diameter of a human hair. These particles are generated from vehicle emissions, diesel engines, and burning wood. In 1995, some 700 deaths in Chicago were attributed to a July heat wave, said Dominici. By 2081, a hot spell could kill between 2,100 and 17,500 people there, she said—a figure that can't be attributed only to a larger population.

Dominici and her colleagues developed the models by studying recent weather records, environmental trends, and Medicare data. In Chicago, they found that hospital admissions for heat stroke between 1987 and 2005 “identified a heat wave much better than the temperature [readings].”

—John Dillon



PAUL OFFIT

“Good science has won out”

The controversy over childhood inoculation came to Yale when audience members confronted an expert who declared that the anti-vaccine movement is “fraying at the edges.”

For 30 years news articles have blamed vaccines for serious defects in children, leading parents to refuse inoculations for their children, said Paul A. Offit, M.D., chief of the Division of Infectious Diseases at Children's Hospital of Philadelphia and author of the 2008 book *Autism's False Prophets*. Though inaccurate, those articles are effective, he said, because “we're very much moved by emotion.” But “the pendulum is swinging back,” said Offit, who delivered the Beaumont Lecture in January.

When anti-vaccine blogger Jake Crosby tried to ask a question, Offit accused him of stalking him and asked him to leave. After Crosby left, Mary Holland, co-author of a book questioning vaccine safety, told Offit he was “not willing to engage” with critics.

Offit said that “good science has won out.” A turning point occurred in January 2011, when an editorial in *BMJ* (formerly the *British Medical Journal*) called articles by a British physician that linked autism to the MMR vaccine an “elaborate fraud.”

Offit urged vigilance to prevent the anti-vaccine movement—and largely forgotten childhood diseases—from re-emerging. “Never let anything go unchallenged,” he said.

—J.D.

World War I sacrifices for a greater good

Government posters urged Americans to save food for troops and for civilians in war-torn Europe.

By Jill Max

The image is haunting: against a background of imploring children with outstretched arms, a gaunt woman cradles an infant in one arm and holds a little girl close with the other. Although it looks like a museum-worthy work of art, this picture on a World War I poster exhorted viewers, “Don’t waste food while others starve!”

One week after entering the war in April 1917, the U.S. government established a Committee on Public Information (CPI) to involve the nation in the war effort. The committee’s materials included a poster campaign designed to help the U.S. Food Administration, headed by Herbert Hoover, in its drive to feed the troops and ensure an adequate food supply for the civilian population at home and abroad. “It was considered effective at instilling patriotic feelings and actions of self-sacrifice,” said Susan Wheeler, curator of prints and drawings at the Cushing/Whitney Medical Library, which displayed Yale’s collection of World War I food posters in the fall of 2011.

The poster campaign was overseen by the Division of Pictorial Publicity, led by Charles Dana Gibson, one of the best-known artists of the time and creator of the Gibson Girl. The division invited other top artists and illustrators

to contribute designs. Every Friday the group and government officials met over dinner to decide what kind of poster was needed. By the end of the war, 700 poster designs had been submitted on a variety of topics, including food. The cost to the government was only \$13,000, as the artists donated their time and materials.

George Creel, a Denver journalist who chaired the CPI, later recalled, “I had the conviction that the poster must play a great part in the fight for public opinion. The printed word might not be read, people might not choose to attend meetings or to watch motion pictures, but the billboard was something that caught even the indifferent eye.” Indeed, because the posters were widely displayed in shops, schools, and other locations, it was impossible to escape their messages.

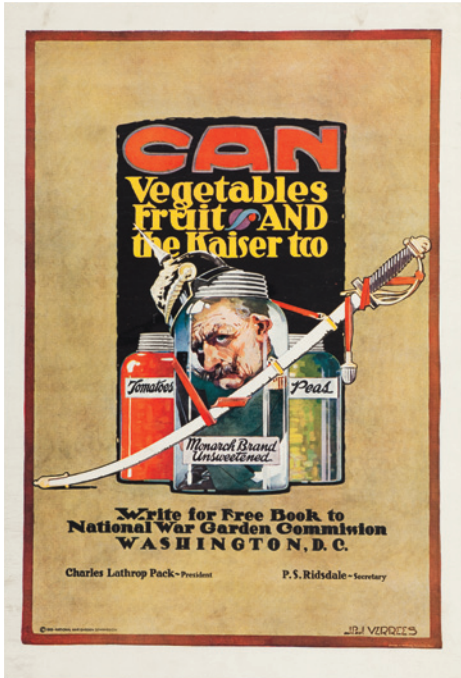
The earliest CPI posters were simple text designs instructing the public not to waste food, with tips on which items to conserve to “serve the cause of freedom.” Such famous figures as Abraham Lincoln, Woodrow Wilson, and Joan of Arc appeared as symbols of patriotism and self-sacrifice.

Images from the front lines helped the public visualize the ravages of war-torn Europe. Eight artists commissioned as captains accompanied the American Expeditionary Forces overseas and produced more than 300 drawings, including scenes of a food convoy winding through a snowy landscape and an American soldier standing over a fallen German. These images helped the

public understand how small sacrifices at the dinner table might be transformed into meaningful contributions to the war effort.

Food posters were tied to such other media as pamphlets, films, poetry, and music. In his poem “Thoughts Inspired by a War-time Billboard,” Wallace Irwin memorialized a poster by the artist Wallace Morgan in the line “Wallie Morg’s ‘Feed a Fighter’ lurks deep in his trench....” The popular marching song, “We’re Off to Can the Kaiser,” was adapted by the Belgian artist J. Paul Verrees for one of the best-known posters of the National War Garden Commission, which urged citizens to “Can Vegetables, Fruit and the Kaiser Too.” The poster was reissued in 1919 after the end of the war with the heading, “The Kaiser Is Canned.”

The medical library’s 10 food posters are part of its larger collection of about 500 posters related to public health and nutrition. They can be viewed online at <http://cushing.med.yale.edu/gsd/cgi-bin/library?p=about&c=mdposter>.

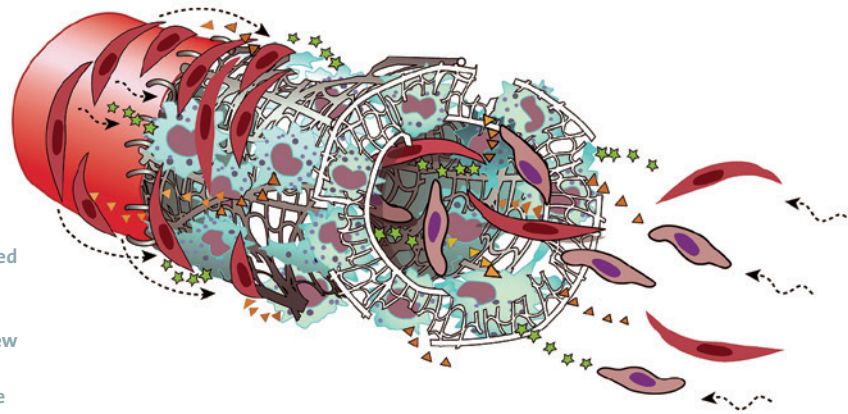
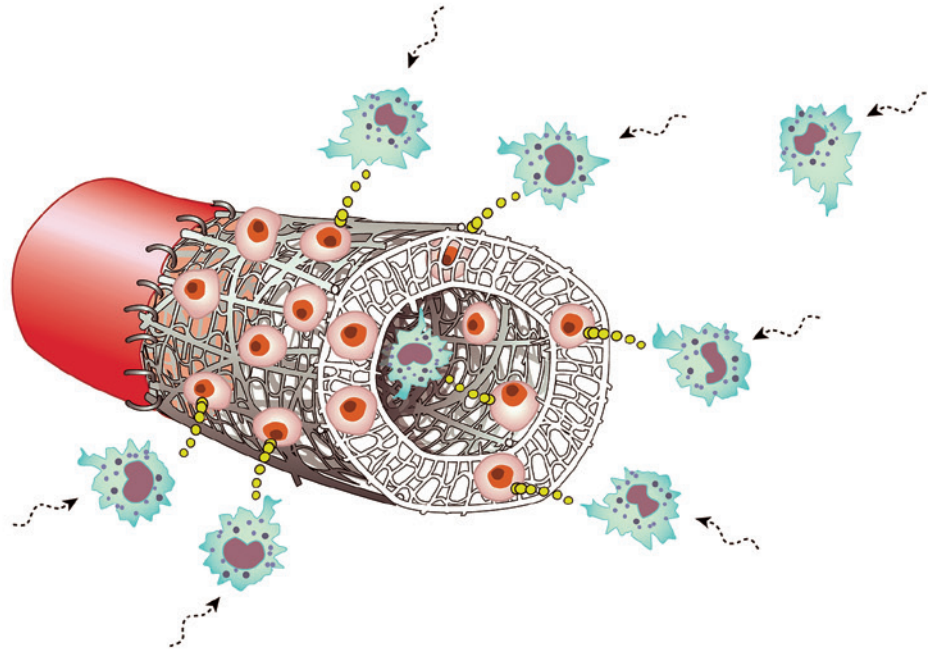


During World War I the U.S. government tried to involve the public in the war effort by urging people to save food for troops and civilians in Europe. The earliest posters offered tips on ways to avoid wasting food, and evoked such figures as Abraham Lincoln, Woodrow Wilson, and Joan of Arc. The artists who created the posters were among the best-known of their day, including Charles Gibson, creator of the Gibson Girl. They donated their time and talents to the war effort.

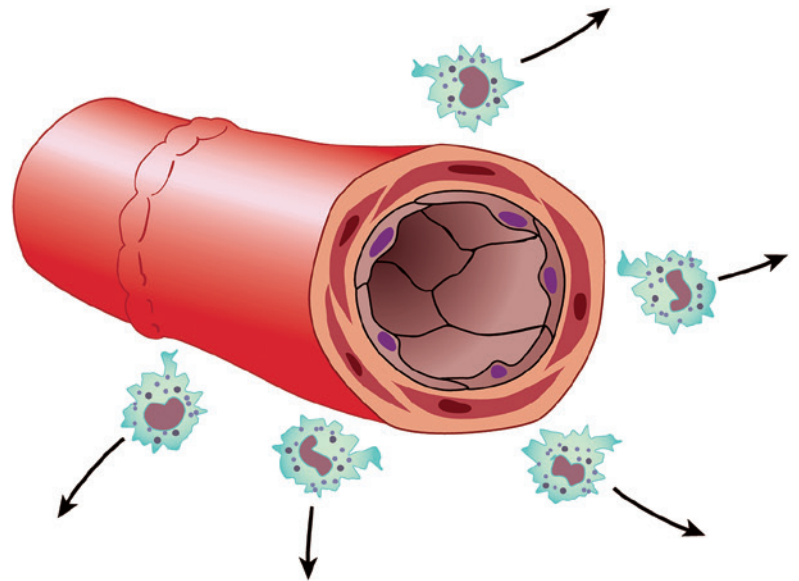


CUSHING/WHITNEY MEDICAL LIBRARY





Pediatric surgeons Christopher Breuer and Toshiharu Shinoka used biodegradable tubular scaffolds seeded with a young patient's bone marrow cells to engineer new blood vessels. The bone marrow cells disappear, but first stimulate an inflammatory response that attracts immune cells to the graft (top). The immune cells then attract epithelial and smooth muscle cells to the dissolving graft (middle) that eventually form the new vessel (bottom).



Tissue from the lab mends a broken heart

A 3-year-old Bridgeport girl becomes the first patient in the United States to receive a bioengineered blood vessel.

By John Curtis

Angela Irizarry was still in her mother's womb when tests revealed that one of her heart's two ventricles wasn't working. She was destined to be a "blue baby." With only one functional ventricle, oxygenated and deoxygenated blood would mix within that ventricle, causing hypoxia and the bluish coloration of the skin that gives the syndrome its name. In 1968 a surgeon named Francis Fontan, M.D., devised a procedure that has become the standard of care to palliate this condition. It involves three surgeries to redirect blood flow: one a few days after birth; a second a few months later; and a third when the child reaches the age of three. In that final procedure a plastic tube is inserted to channel blood from the inferior vena cava to the lungs. For Angela, however, surgeons had something different in mind. She would undergo the first two surgeries as usual—but for the third, a biodegradable scaffolding seeded with cells from her own bone marrow would replace the plastic tube. She would be the first patient in the United States to receive a bioengineered cardiac blood vessel.

A meeting at MIT

On the window sill of his office in the Boardman Building, Toshiharu Shinoka, M.D., PH.D., keeps a photo of his days as a postdoctoral fellow in Boston in the 1990s, where he met his friend and colleague, Christopher K. Breuer, M.D. Also in the group photo are Joseph P. Vacanti, M.D., an expert in tissue engineering; and Robert Langer, PH.D., the MIT professor

renowned for his innovative medical devices. Shinoka, associate professor of surgery and pediatrics and director of pediatric cardiovascular surgery, and Breuer, associate professor of pediatric surgery and pediatrics, met while studying under Vacanti and Langer at Children's Hospital Boston.

"What made me become interested in tissue engineering was the fact that on a daily basis in my training I would see problems arise that we couldn't fix. I would watch children die and watch families fall apart. That obviously left a bad taste in my mouth," said Breuer. "In surgery there are many problems we could fix if we had adequate tissue. Tissue engineering provided means of creating an abundant source of tissue for surgical reconstructive procedures."

The pair first attempted to engineer intestines, but found that the science of the day was not up to the task of producing such complex tissue. They switched to blood vessels and found a technique that worked. They created a biodegradable scaffolding with a matrix for seeding cells as well as sites for cell attachment and tissue formation, then implanted it in a lamb. "The scaffolding degrades and the remaining tissue is viable and it's made from people's own tissue, so you can avoid problems like rejection," Breuer said.

But problems remained. "Using our original method it took three months to grow the cells, and seed, and incubate the scaffold. Surgeons don't have three months to wait for a blood vessel," Breuer said. Waiting that long also

increased the odds of contamination and the risk of evolution running its course—cells in culture could differentiate and change their identity or even become tumor cells.

The collaboration ended when Breuer entered the U.S. Air Force and Shinoka returned to Tokyo Women's Medical University Hospital to continue his research. He switched from blood vessel cells to bone marrow cells, which are so abundant that they don't need to be grown in culture. That cut the time needed to make the grafts from a few months to a few hours. Shinoka began implanting the biodegradable grafts in humans with promising results.

When Breuer heard of Shinoka's success he was still in the military and attending to injured veterans of the war in Afghanistan. "It was one of those days in your life where you get hit by lightning," Breuer said. "I just knew what I was going to do with the rest of my career."

By 2003 Breuer had moved to Yale, lured by a new tissue engineering initiative and faculty, including W. Mark Saltzman, PH.D., chair and Goizueta Foundation Professor of Biomedical Engineering and Chemical and Environmental Engineering, who had also trained under Langer at MIT; Jordan S. Pober, M.D. '77, PH.D. '77, HS '78, Ensign Professor of Immunobiology, professor of dermatology and of pathology, and director of the Human and Translational Immunology Program; and William C. Sessa, PH.D., Alfred Gilman Professor of Pharmacology and director of the Vascular Biology and Therapeutics Program. "It was a wonderful environment in which to perform translational research," Breuer said.

Three years later he urged Shinoka to join him. "It was very suitable for our future research so I decided to come over here," Shinoka said. "In the United States no one was doing this kind of approach."

Rearranging the heart

"When I was five months pregnant they asked me to have a test because I was 37 years old and there was a risk that the baby would have defects," recalled Claudia Irizarry, Angela's mother. She works as a secretary in a church; her husband, Angel, is a contractor. "They figured out that all her organs were backwards. In the same ultrasound they saw that she had this heart condition. Right away they told me that she was going to need three surgeries."

Congenital heart disease is a common birth defect, occurring in one in 100 live births. Single-ventricle physiology, a relatively uncommon subcategory of congenital heart disease, stems from several heart anomalies but leaves children with only one functional ventricle. One of the two ventricles may be larger than the other, or there may be no wall between the two ventricles. These defects force the functioning ventricle to do the work of two, pumping blood for both the lungs and the rest of the body. It also mixes oxygen-rich blood leaving the lungs with deoxygenated blood from the veins from the lower body, leading to the "blue baby"

syndrome. Without surgical intervention, about 70 percent of children with the defect die in the first year of life. Few reach adulthood. The Fontan procedure, though palliative rather than curative, has been the only solution.

"What this operation did was rearrange the plumbing, so that that one ventricle could pump blood to the body, and then that blood would return and go through the pulmonary circulation passively, without a ventricle pushing it through. This prevented the mixing of blood so the children were no longer cyanotic," Breuer said.

Despite its benefits, the Fontan procedure posed problems. It required the use of synthetic materials that could lead to blood clots and other complications. It also meant a lifetime of blood-thinning drugs for the patients. The synthetic grafts left children vulnerable to infections. And the grafts could not grow with the children. "Children can outgrow their operations, just the way they can outgrow their shoes. Imagine living in a world where every time you outgrow your shoes you have to go back to the operating room," Breuer said.

Angela would receive a biodegradable graft—a scaffolding made with bioengineered tissue seeded with cells from her bone marrow. It would connect the inferior vena cava—the vein that transports deoxygenated blood into the heart's right atrium—with the arteries that carry blood to the lungs. She would require neither immune suppressants nor blood thinners. The bioengineered graft would also reduce the risk of infection. The operation would raise Angela's oxygenation level, give her more energy, and lead to better growth and development.

"We wanted to choose the right patient for undergoing this procedure. Just as important, we wanted to find the right family," Breuer said. "We talked to a number of people but felt the Irizarry family were quite a special family. They were probing and they asked appropriate questions."

Building a blood vessel

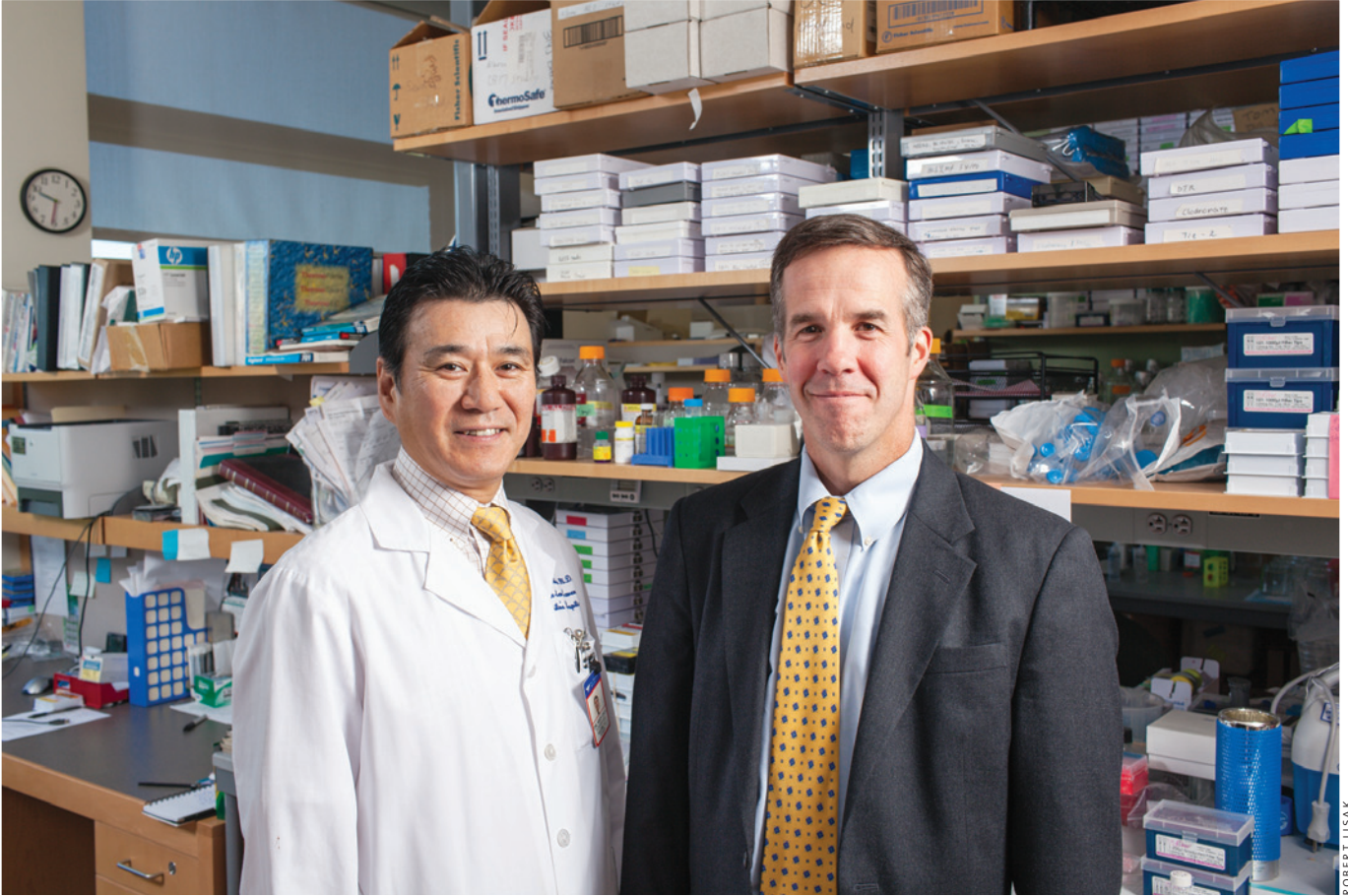
Shinoka had used his technique in 25 patients in Japan. But when it came time to seek FDA approval, there were questions about how it worked. The FDA wanted to know what was happening during the graft's formation and why. The answers would take years to find and fill 3,000 pages.

Shinoka and Breuer believed at the time that bone marrow cells were a source of stem cells that turned into blood cells. But the bone marrow cells they were seeding onto the grafts disappeared after a week. They repeated the experiment, with the same results. If the stem cells were differentiating into blood cells, why did they vanish? After more experiments, which involved inserting a fluorescent dye into the cells so they could be tracked in mice, the researchers realized that even though they were getting the right result, they had misunderstood the mechanics of what was happening. The stem cells were not engineering new tissue. Rather, the stem cells were using molecules typically seen in



JOHN CURTIS

Angela Irizarry, now 4, shown with her mother Claudia, is the first patient in the United States to receive a bioengineered heart vessel. Angela was born with only one functioning heart ventricle.



Toshihara Shinoka and Christopher Breuer met in the 1990s as post-docs at MIT, where they shared an interest in creating bioengineered tissue for use in surgery. Now both are at Yale, where they worked on the first implantation of a bioengineered heart vessel in the United States.

inflammation to induce cells to leave nearby blood cells and regenerate. “It was much like how a salamander regrows its tail, or a starfish regrows an arm that’s been cut off,” Breuer said. “The scaffolding enabled the body to recreate a blood vessel. It enabled us to identify some of the molecular signals that were really important for this process, which we could then manipulate in our model systems.”

“It’s a milestone in tissue engineering,” said Gary S. Kopf, M.D., professor of surgery, who performed Angela’s surgery with Shinoka. “Dr. Breuer and Dr. Shinoka’s lab work is pioneering in terms of working out the mechanism of how tissue-engineered blood vessels form.”

“Moving this to the clinic is clearly a landmark accomplishment,” said Langer, the MIT professor. “This is a very significant achievement, that they have been able to take this very basic work in the laboratory and test it in people. You need to get the right biocompatibility. You need the right mechanical properties. You have to make it cell-compatible. You have to do it in such a way that there are no foreign body reactions.”

Between the lab and the operating room

The surgery began at 6 a.m. on a morning in August 2011, when the surgeons aspirated Angela’s bone marrow. They needed 5 ccs of bone marrow for each kilogram of her body weight, between 55 and 70 ccs total. The operating room team included two attending surgeons, one surgical fellow, two anesthesiologists, two perfusionists, and two nurses. A five-minute walk away in the Richard D. Frisbee III Laboratory of Stem Cell Transplantation and Hematopoietic Graft Engineering, five postdoctoral fellows seeded the scaffolding with Angela’s bone marrow—a three-hour procedure. The timing had to be just right. The seeded scaffolding had to be ready when the surgeons needed it so as not to prolong the surgery. Before the operation the team practiced preparing the scaffolding more than 20 times with bone marrow purchased from a blood bank, Shinoka said. “We had stopwatches and we were trying to save every second we could,” Breuer said.

In addition, per FDA regulations, more than 10 tests had to be performed on the graft before it could be implanted to ensure that it was neither toxic nor infected.

While the fellows were preparing the graft, Shinoka and Kopf were in the operating room, preparing Angela’s heart. They needed about two hours to remove scar tissue from her previous surgeries. Throughout the operation the surgical team was in contact with the hematology fellows preparing the graft. “We were communicating every 30 minutes. The timing was pretty good,” Shinoka said.

Once the surgeons had the graft, which measures 18 mm in diameter by 4 to 5 centimeters in length, they connected Angela to a cardiopulmonary bypass machine for an hour while they implanted it. The entire operation lasted about eight hours.

The procedure, said Kopf, follows the path of the traditional Fontan procedure. “It is the same exact surgery,” he said, noting the one difference. “Instead of using a piece of plastic, usually Gore-Tex, we used the tissue-engineered graft. In terms of the surgery, I would say it is a little easier to use. It is thinner and more flexible and seems to hold the sutures very well. It doesn’t seem to have any bleeding, and the Gore-Tex does have a little more bleeding.”

Angela is not only the first patient in the United States to receive a bioengineered blood vessel but also the first of six patients participating in a five-year clinical trial. Breuer and Shinoka will monitor her for three years after her surgery. They will watch for complications from the graft and determine whether the graft does in fact grow with the child. Over time the surgeons plan to measure its size and compare it to normal blood vessels.

“We have taken a very cautious approach,” Breuer said. “We wanted to learn as much as we could from each patient before we went on to the next patient. We will do one patient, wait for six months; do two patients, wait six months; do three patients, wait six months.”

A child’s recovery

So far the surgeons have been pleased with Angela’s recovery, as have her parents. Angela has reached all her post-operative milestones, Breuer said. “The last time I saw her in clinic she was a normal 3-year-old running around. I think Angela will be a very normal child.”

“Before when she wanted to run with her brother, she got tired,” said Claudia Irizarry. “Now, she doesn’t want to stop. She can keep going. Her oxygen level is very, very good now.”

On a chilly day in December, Claudia kept her daughter inside, even though she’s strong enough to play outside and ride a bicycle. She has never attended day care or school, nor can she play with children other than her brother, because during her recovery she’s still susceptible to infections. At home, where she lives with her parents, brother, and grandmother, Angela likes to play games on the computer, watch Scooby-Doo on television, and curl up in her mother’s lap.

“If God sent me the baby, God also sent me the angels to care for her,” Claudia said. “I always believed that everything was going to be okay. She is very positive. She’s very happy. My hope for her is the same that all moms have, that she can do whatever she wants, that she can grow up and be a good person. I tell her I hope she grows up to be a doctor, to help kids the same way they helped her.” **YM**

John Curtis is the editor of *Yale Medicine*.

BELOW Lee Cruz, a community outreach director at the Community Foundation for Greater New Haven, led Robert Wood Johnson Foundation clinical scholars on a tour of New Haven's Fair Haven neighborhood last summer. At the start of each academic year scholars visit the areas

where they will be doing research that will benefit local communities.

RIGHT Scholar Oni Blackstock, center, at a seminar with fellow scholars. Blackstock worked with a New Haven community group on food issues.





JOHN CURTIS (2)

Scholars work toward healthy communities

Yale's Robert Wood Johnson Clinical Scholars make a point of engaging the community in their research and making the world a healthier place.

By Jennifer Kaylin

When Oni Blackstock, M.D., arrived in New Haven in the summer of 2010 to begin her fellowship as a Robert Wood Johnson Foundation (RWJF) Clinical Scholar, she and some of the other fellows took a walking tour of the city's West River neighborhood—home to many of the patients treated by Yale physicians.

"I was really excited," says Blackstock. "I know a lot of people who have spent years in New Haven and have never gone to these communities. I think it's really important to get a sense of the reality of your patients' lives. You don't get that just seeing them in the office."

The tour served its purpose. Blackstock saw the urban neglect, the effects of unemployment, lack of access to healthy foods, limited recreational facilities, and the residents' reliance on public transportation. She also saw, in the community leaders who led the tours, the neighborhood's strength and resiliency. What Blackstock didn't see, at least initially, was how what she learned on the tour would dovetail with her own clinical interests, inform her work as an RWJF fellow, and most likely influence her medical career well into the future.

As the tour was winding down, the scholars were taken to a meeting of the West River Neighborhood Services Corporation. Community residents had gathered to discuss a number of issues, including where they were going to buy their food now that the Shaw's Supermarket chain had closed its store on Whalley Avenue.

“As a primary care doctor I care a lot about food insecurity and its health consequences, and I knew that we would be able to help the West River residents in some capacity,” says Blackstock, who attended Harvard Medical School.

With the loss of Shaw’s, community organizers were weighing other food distribution options—possibly a food co-op, another supermarket, or a buyers’ club—but first they needed to figure out what neighborhood residents want and would be prepared to support. Blackstock and Jed Barash, M.D., a first-year scholar, worked with neighborhood corporation members to develop a survey tool to gauge community needs and feelings.

Although a Stop & Shop supermarket has recently opened in the old Shaw’s site, Blackstock says strong support remains for an alternative. Their survey specifically asked whether Stop & Shop satisfies the neighborhood’s grocery needs. Noting that some residents expressed concern about Stop & Shop’s prices, she said, “We believe affordable quality food remains a need, even with the presence of Stop & Shop.”



ABOVE & RIGHT Scholars Clara Filice and Gregg Furie are examining the public health impacts of a plan to fill in the Route 34 Connector and build apartment buildings and office space above it.

TOP Such urban issues as pedestrian safety, gun violence, motorcycle safety, and access to affordable food, have been subjects for research by clinical scholars.

This finding is something that wouldn’t be known without engaging the community. Replacing one large supermarket with another would seem to be the ideal solution—but when residents were surveyed, a different picture emerged.

“When the research is generated by the community, it’s a more holistic, honest, and genuine way to approach research,” says Blackstock. “Forming these partnerships helps community members understand what research is, and it builds a bond between academia and the community.”

This bonding, administrators of the Yale RWJF Clinical Scholars Program would say, is exactly how their program is supposed to work. “What we’re aiming for is alignment of the scholars’ passions and the needs of the community they are serving,” says Marjorie Rosenthal, M.D., M.P.H., the program’s assistant director.

Such community-based participatory research is an important facet of the program, says Program Director Harlan M. Krumholz, M.D., the Harold J. Hines Jr. Professor of Internal Medicine. “We have maintained our traditional commitment to teaching core competencies in research and enriched our curriculum with this work. We are a program that trains people for a variety of roles in a range of organizations, but we are trying to change the paradigm of research too—with an emphasis on thinking about the end-user of the knowledge.”

People who ask the next question

In 1973, Yale was one of the founding sites for the nascent RWJF Clinical Scholars Program, a two-year fellowship that teaches research skills, health policy, leadership, media/communication skills, and community health. The other three sites



are the University of Michigan, the University of Pennsylvania, and the University of California, Los Angeles.

Young doctors apply for RWJF fellowships after they've completed their residencies, with seven or eight scholars a year being accepted into the Yale program. Upon successful completion of the program, they receive the degree of Master of Health Sciences Research.

Rosenthal said that the ideal clinical scholar candidate is someone who is interested in the interplay between research and policy. "We're looking for people who, when they're on rounds, are continually asking the next question," she says. "If the patient has anemia, they're not satisfied asking, 'How should we treat this?' They want to know why the patient has it; is there something about the social structure that contributed to this?"

Krumholz adds that the successful RWJF scholar is willing to challenge the conventional wisdom. "Just because that's the way things have been done for a long time doesn't mean it's the right thing," he says. "The inclination is to just go along. We want critical thinkers who have the courage of their convictions."

The program is divided into a didactic year followed by a year devoted to research. Coursework includes training in clinical epidemiology, community-partnered research, health economics, health policy, health systems management, organizational behavior, and leadership development. The four foundational courses are biostatistics; clinical and health services research methods; principles and processes of community-based research approaches; and principles of health policy and management.

Central to scholars' training is the expectation that they will conduct two or more health services research projects during their fellowship and contribute to scholarship in clinical research. They are encouraged to undertake at least one project that involves primary data collection and tackle projects that use different methodological approaches. Scholars are also expected to maintain their clinical skills through interactions with patients at Yale-New Haven Hospital, the VA Connecticut Healthcare System in West Haven, or affiliated clinic, hospital, or community-based health centers.

To date, 151 scholars have graduated from the Yale program, with seven more graduating in 2011. Graduates work in a wide range of jobs in academia and politics as well as holding other positions in the public, private, and nonprofit sectors. Stephen Cha, M.D., FW '06, is the chief health care policy advisor to U.S. Representative Henry Waxman, D-Calif.; Katherine Goodrich, M.D., FW '10, is the chief medical officer of the Office of Planning and Evaluation at the U.S. Department of Health and Human Services; David M. Krol, M.D., FW '01, is the team director and senior program officer of human capital at the Robert Wood Johnson Foundation; Eric S. Holmboe, M.D., PH.D., FW '98, is the chief medical officer and senior vice president of the American Board of Internal Medicine; and Anu Gupta, M.D. '97, HS '00, FW '02, oversees the HIV/AIDS

philanthropic portfolio of Johnson & Johnson's Corporate Contributions Division.

A move to community-based research

The original program's stated mission, according to Krumholz, was training fellows to be "skilled in clinical research to the same extent that people were in basic sciences," and to understand research methods, develop fluency in the language of clinical research, and become astute readers of the scientific literature. "Our ulterior motive," he adds, was to sharpen critical thinking skills. "We wanted them to be able to pinpoint the key leverage points in medicine and make a difference."

The founding director of Yale's clinical scholars program was the late Alvan Feinstein, M.D., Sterling Professor of Medicine and Epidemiology. Under his direction the Yale program developed a reputation for excellence in training its scholars in clinical research methods. As the RWJF program matured both nationally and at Yale, however, its mission evolved. In the most recent funding cycle, which began in 2005, national directors maintained the rigorous training in research methods, but added a new emphasis on community-based participatory research.

"We fully embraced the idea," says Krumholz. "Too often we're doing research without soliciting input from the people we're seeking to help." Krumholz calls the result "con-fetti papers"—research papers that are published, maybe even attract some press coverage, but generate "no conversation." He says this lack of feedback usually occurs because there wasn't enough front-end work with the end-users. "Other researchers may cite the paper," he said, "but that doesn't matter if it doesn't lead to action."

Now, six years into the latest funding cycle, Krumholz calls Yale's community-based participatory research initiative "the jewel of our program." At least 15 percent of the scholars' time is devoted to research in partnership with organizations serving New Haven. The work is guided by the Steering Committee on Community Projects, composed of a cross-section of community representatives and Yale affiliates working with the New Haven community. So far, seven projects have been completed and disseminated; another 10 are either under way or being planned.

Yet in the beginning it was far from a given that community leaders would agree to partner with the scholars. "People were suspicious when we proposed this," Krumholz recalls. "They'd had people like us approach them before and write them into their grants, only to lose interest in them as soon as the grant came through. I made a personal promise that we wouldn't abandon them—that this was a sincere, genuine offer."

New Haven's size and demographics make it an ideal place to conduct community-based participatory research, says Georgina Lucas, M.S.W., deputy director and steering committee chair of the Yale RWJF clinical scholars program. "It's a microcosm of a much larger urban area," she said. "You can

get your arms around it, and it's small enough that you can build relationships and disseminate information."

The challenge, she adds, is completing a project within the two years the scholars are in the program. "People don't realize how much time community research takes," she says. "You need to engage your stakeholders to get complete and accurate information and to create effective and sensitive interventions, but that means building relationships and trust—which takes time."

Gun violence and motorcycle helmets

When Chisara N. Asomugha, M.D., M.P.H., FW '09, was in the program, her community-based participatory research focused on youth-related gun violence in New Haven. Working with the New Haven Family Alliance, she used an established research approach called Photovoice to collect data. New Haven youths between the ages of 14 and 19 were given cameras and asked to photograph scenes reflecting their community's strengths and challenges. The photographs were then used as a stimulus for focus group discussions with an eye toward gaining insights into local policy and service needs.

After the project was completed, the photographs were displayed in the New Haven Public Library, while Asomugha, who attended the Duke University School of Medicine, shared her final report with Mayor John DeStefano Jr. Soon afterward she was hired as New Haven's deputy mayor for community services.

Gregg Furie, M.D., drew inspiration for his community research project from the city's plan to remove the Route 34 Connector in an effort to reconnect the medical campus and adjacent neighborhoods with the rest of the city. He's been working with fellow scholar and pediatrician Clara Filice, M.D., and the city's health, planning, and economic development departments to conduct a health impact assessment that will focus on pedestrian and bicycle safety, activities for walkers, and reducing accidents. "It's a way to introduce health as a consideration in public policy decision making," says Furie, who got his medical degree from Harvard. "City planning and public health have different objectives, so we're trying to make sure the public health impact doesn't get lost."

In talking about their research projects, all the scholars say they are gratified to have the opportunity to contribute to addressing real health needs; but they also recognize that through the cultivation of personal relationships with community members and the process of consensus building—which is so important for the success of a community project—they are developing other skills that will be valuable in their later careers.

Adam Landman, M.D., FW '10, wanted to do a research project on the correlation between wearing a motorcycle helmet and serious injuries. Krumholz questioned whether the topic might be too obvious—of course wearing a helmet reduces the likelihood of serious injury.

"One of the most beneficial parts of the program," Landman says, "is learning to clearly articulate the importance and value of the research you're doing." In the case of the helmet study, Landman and Michael Phipps, M.D., his RWJF partner, were able to persuade their professors and colleagues that the project was worthwhile. "We knew from the outset that the results wouldn't be novel," Landman says, "but we were okay with that. There had been discussions in the past about making helmet use mandatory in Connecticut, but there was no recent data to inform the decision making. Our goal was to use our research skills and rigorous methodology to inform an important public health topic."

In her new job as deputy mayor, Asomugha is already seeing the value of acquiring a deeper understanding of the social determinants of health that she gained through her training as a clinical scholar. She cites an incident she says is not atypical, concerning a woman who had been scrupulous about getting her daughter to her medical appointments. "They rode their bikes and were always on time," Asomugha says. "After one appointment, the doctor gently told the mother that her child should wear a helmet when bike riding. The woman missed her next appointment, and the doctor didn't know what had happened." Upon hearing the story, Asomugha quickly understood—the mother couldn't afford a helmet. Embarrassed and unwilling to risk what she saw as further rebuke, she skipped her appointment. "It's the unintended consequences of trying to do a good thing," Asomugha says. "It's very common, and it's something we need to try to anticipate and avoid."

Peggy Chen, M.D., FW '10, learned a similar lesson during her time in the clinical scholars program. She was helping the New Haven Healthy Start Program Consortium develop a brochure about obesity and the importance of exercise and healthful eating.

"We came up with an initial draft and thought, 'This is great. They're going to love it,'" Chen says. "They changed every word and all the photos." The problem, Chen came to learn, was that the brochure, complete with photos of overweight women standing on scales, had the scolding tone of a finger-wagging gym teacher. "You'll get high blood pressure; you'll get diabetes, blah, blah, blah. These women have gotten negative messages from everywhere else. They didn't need another one from us." The new draft, which emphasizes all the positive things that can happen when one lives a healthful lifestyle, was quickly approved.

The community takes notice

It's not just the scholars who see the value in the program's community research component; community partners in New Haven and RWJF's national program office have also taken notice.

Rebecca Allen, director of programs and services for the Columbus House homeless shelter, remembers when Ryan



Greyson, M.D., a RWJF scholar, contacted the shelter's executive director, Alice Cunningham. Greyson's project was to find ways to improve communication between the shelter and Yale-New Haven Hospital. "We get lots of people coming through here wanting to talk or do research," she says, "but Ryan brought it to a whole new level. He partnered with clients and staff. He gave us feedback and held our hand every step of the way. Usually doctors don't speak our language, but Ryan does. He's always very understandable and approachable."

Desmond Runyan, M.D., D.P.H., the RWJF national program director, was even more effusive. "The Yale program is doing exceptional work in the community," he says. "Harlan and his staff are doing a superb job." This finding is all the more noteworthy, he adds, because Yale hasn't always enjoyed the most collaborative relationship with its host city. "Yale has a reputation for having a town/gown split, so it's remarkable how strong the ties are now, how invested people have become. Overall, the success of community-based research is best exemplified in Yale."

Runyan also cites Yale's leadership component as an area where it excels. About four years ago, under the stewardship of Irwin Birnbaum, J.D., the medical school's former chief operating officer, and David Berg, Ph.D., clinical professor of psychiatry, the clinical scholars program began offering seminars in leadership development and organizational management. Scholars are given an opportunity to shadow health industry leaders and attend group discussions when such leaders come to campus.

But in this latest iteration of the clinical scholars program, it is the commitment to community-based participatory research

LEFT Clinical scholars helped organize a farmstand in the West River neighborhood. The stand, operated by CitySeed, opened in July 2011. CitySeed outreach coordinator Cara Donovan (left) sold fresh vegetables to residents.

ABOVE TOP Harlan Krumholz, director of the scholars program, led a seminar with scholars in October.

ABOVE Clinical scholar Oni Blackstock (right) worked with community groups in New Haven's West River neighborhood on issues including access to healthy food. She joined, from left, community partner Ann Greene, scholar Jed Barash, community partner Stacy Spell, and community organizer Billy Bromage.

that is exciting the scholars, winning over hearts and minds in the community, and impressing the program's national administrators who make those all-important funding decisions.

Whether it's helping establish Project Access, a new program that helps the uninsured gain access to health specialists; helping Integrated Refugee and Immigrant Services assess the health needs of new refugees and develop interventions; or designing a method to evaluate the progress made on Mayor DeStefano's Teen Pregnancy Prevention Council, Yale's clinical scholars are collaborating with community members to address their neighbors' health needs in the hope of changing their circumstances. If their work proves to be valuable beyond New Haven, so much the better.

"At the end of our lives and careers, to just look back on a big curriculum vitae would be a shame," Krumholz says. "We should strive to leave a legacy of better health in the community." **YM**

Jennifer Kaylin is a writer in New Haven.



Peter Schulam

New urology chair named

PETER G. SCHULAM, M.D., PH.D., was named chief of the Department of Urology at Yale-New Haven Hospital and chair of the department at the School of Medicine in January. Urology, previously a section within the Department of Surgery, has recently been elevated to departmental status.

Schulam comes to Yale from the Ronald Reagan Medical Center at UCLA, where he was vice chair of urology, chief of the division of endourology and minimally invasive surgery, and director of both the kidney stone treatment center and the surgical living kidney donor program.

Schulam has long-standing clinical interests in adrenal disorders; bladder, prostate, and kidney cancer; donor nephrectomy; and kidney stones and kidney reconstruction. He is nationally known for his expertise in minimally invasive surgery and laparoscopic techniques.

A native of New Haven, Schulam received his medical degree as well as his PH.D. in immunology at Baylor College of Medicine in Houston.

He replaces Robert M. Weiss, M.D., the Donald Guthrie Professor of Surgery (Urology), who has led the Section of Urology within the Department of Surgery. Weiss will continue his laboratory research and his active urology practice.



Richard Edelson

National Physician of the year

RICHARD L. EDELSON, M.D., '70, chair and the Aaron B. and Marguerite Lerner Professor of Dermatology, was one of five physicians to receive a National Physician of the Year Award from Castle Connolly Medical Ltd. in March. Edelson is an internationally recognized pioneer in the research and treatment of cutaneous T-cell lymphoma (CTCL), a cancer affecting the skin. He identified and characterized this cancer, and his research group played a central role in deciphering the basic properties of CTCL cells in order to develop effective therapies. Edelson, who served as director of the Yale Cancer Center, received a Clinical Excellence Award. Castle Connolly Medical Ltd. publishes guides to the best doctors in the United States.

Edelson developed extracorporeal photochemotherapy (ECP) for CTCL patients in clinical trials at Yale Cancer Center. ECP, the first FDA-approved selective immunotherapy for cancer, has been used more than 3 million times worldwide to treat CTCL, organ transplant rejection, and graft-versus-host disease, the major complication following bone marrow transplantation.

Edelson, who served as director of the Yale Cancer Center, received the Clinical Excellence Award at a ceremony in March. Castle Connolly Medical Ltd. publishes guides to the best doctors in the United States.



Melissa Grafe

Historical librarian appointed

MELISSA J. GRAFE, PH.D., was named the John R. Bumstead Librarian for Medical History at the Cushing/Whitney Medical Library last year. Grafe replaces Toby A. Appel, PH.D., M.L.S., who retired in 2010. Grafe, whose doctorate is in the history of medicine, comes to Yale from Lehigh University, where she was the humanities librarian. For her doctoral research at Johns Hopkins she specialized in 18th-century American medical practice, but she also worked with rare books and special collections at the Historical Collection for the Institute of the History of Medicine.

Among her current projects is Yale's participation in the Medical Heritage Library, an effort by leading medical libraries to make rare books accessible online. Collections from Yale, Columbia, Harvard, Johns Hopkins, the National Library of Medicine, the New York Public Library, and other institutions are being digitized and posted online.

"I see my job as working with researchers, students, faculty, and anyone who is interested in the history of medicine and our collections, and helping to bring forth new knowledge," said Grafe, who oversees a staff of four full-time employees, one part-time employee, and three part-time student hires. "We're here to preserve the collection for future generations. We're here to make it accessible either through digital resources or blogs or the exhibitions and classes that we do. We're here to help our patrons."



Tamas Horvath



Gerald Shulman

Two Yale scientists were among 11 to receive Laureate Awards in November from the Endocrine Society, the largest organization devoted to research on hormones and the practice of endocrinology. According to the society, the awards represent the pinnacle of achievement in the field of endocrinology.

Tamas L. Horvath, D.V.M., PH.D., the Jean and David W. Wallace Professor of Comparative Medicine and professor of neurobiology and of obstetrics, gynecology and reproductive sciences, received the Ernst Oppenheimer Award. This award recognizes meritorious accomplishments by a young investigator in the field of basic or clinical endocrinology.

Gerald I. Shulman, M.D., PH.D., the George R. Cowgill Professor of Physiological Chemistry, professor of medicine and of cellular and molecular physiology, and a Howard Hughes Medical Institute investigator, will deliver the Clinical Investigator Award Lecture at the society's annual meeting in June. The award acknowledges major contributions to clinical research related to the pathogenesis, pathophysiology, and treatment of endocrine diseases.

Daniel A. Colón-Ramos, PH.D., assistant professor of cell biology, received the Early Career Award for Public Engagement with Science at the annual meeting of the American Association for the Advancement of Science in Vancouver in February. The award recognizes his work with the nonprofit organization CienciaPR, a website for educators and professionals interested in science and Puerto Rico. The award, established in 2010, is given once a year to an



Daniel Colón-Ramos



John Krystal



Steven Marans



Michael Nathanson



Stanley Rosenbaum



Elisabetta Ullu

early-career scientist or engineer who demonstrates excellence in contributions to public engagement with science activities.

Guadalupe Garcia-Tsao, M.D., professor of medicine (digestive diseases), is the new president-elect of the American Association for the Study of Liver Diseases. Garcia-Tsao is a staff physician at the VA Connecticut Healthcare System, where she is chief of the Section of Digestive Diseases and program director of the Hepatitis C Resource Center. She is also director of the Clinical Core of the NIH-funded Liver Center at Yale. Garcia-Tsao earned her medical degree from the Universidad Nacional Autónoma de México and completed her internal medicine residency and gastroenterology fellowship at the Instituto Nacional de la Nutrición in Mexico City. She completed her training in hepatology at Yale and joined the faculty in 1989.

Linda S. Godleski, M.D., associate chief of staff for education at the VA Connecticut Healthcare System in West Haven and associate professor in the Department of Psychiatry, received the 2010 David M. Worthen Award for Career Achievement in Educational Excellence in October. The award recognizes an employee of the Veterans Health Administration who has made contributions of national significance to education in the health professions.

John H. Krystal, M.D. '84, HS '88, the Robert L. McNeil Jr. Professor of Translational Research and chair of the Department of Psychiatry, was installed as president of the American College of Neuropsychopharmacology in December. He will serve a one-year term, studying the neurobiology and treatment of psychiatric disorders. Krystal is a pioneer in translational neuroscience, which is the effort to link concepts and approaches arising from basic brain research to the study of the neurobiology and treatment of psychiatric disorders. He has applied this strategy to develop and test new approaches to treating schizophrenia, PTSD, alcoholism, and depression. Krystal also directs Yale's Center for the Translational Neuroscience of Alcoholism, which is funded by the National Institute on Alcohol Abuse and Alcoholism, and he is a member of the National Advisory Council on Alcohol Abuse and Alcoholism. He is also a member of the Institute of Medicine of the National Academies.

Steven Marans, M.S.W., Ph.D., Harris Professor of Child Psychiatry in the Child Study Center and director of the National Center for Children Exposed to Violence/Childhood Violent Trauma Center at Yale, was appointed in October to the U.S. Attorney General's National Task Force on Children Exposed to Violence. The task force is part of the Defending Childhood Initiative, whose goals are prevention of children's exposure to violence as victims and witnesses; reduction of negative aftereffects on children exposed to violence; and development of better understanding and increased awareness of this

issue. The task force will identify promising practices, program implementation, and community strategies to prevent and respond to children's exposure to violence.

Steve Martino, Ph.D., associate professor of psychiatry, was appointed chief of psychology for the VA Connecticut Healthcare System in December. The VA's Psychology Service has 49 psychologists on staff; it comprises two predoctoral training programs in West Haven and Newington; clinical and research postdoctoral training programs; and opportunities for research, education, and national service. Martino's research interests include motivational interviewing, clinician training strategies, the science of dissemination and implementation, technology-based approaches to therapy, and curriculum evaluation.

Scott J. Miller, Ph.D., chair and the Irénée du Pont Professor of Chemistry, was recognized as a fellow of the American Association for the Advancement of Science (AAAS) in February. The AAAS cited Miller's "visionary approach to catalysis that has resulted in new types of reactivity and unprecedented selectivity in asymmetric synthesis and natural product modification."

Michael H. Nathanson, Ph.D., M.D., FW '90, professor of medicine (digestive diseases), section chief (digestive diseases), and director of the Liver Research

Center, began a five-year term as editor of the journal *Hepatology*.

Stanley H. Rosenbaum, M.D., professor of anesthesiology, of medicine (pulmonary), and of surgery (trauma), received the Lifetime Achievement Award from the Society of Critical Care Anesthesiologists. The award presentation took place at the society's annual meeting in Chicago in October.

Elisabetta Ullu, Ph.D., professor of medicine (infectious diseases) and of cell biology, was named the winner of the American Society for Biochemistry and Molecular Biology's (ASBMB) inaugural Alice and C.C. Wang award. Ullu received the award for her laboratory's work with the protozoan parasite *Trypanosoma brucei*, which causes African sleeping sickness, to uncover a novel mechanism of gene silencing known as RNA interference. The award honors Ching Chung ("C.C.") Wang, Ph.D., professor of pharmaceutical chemistry at the University of California, San Francisco. Ullu received her Ph.D. from the University of Rome in 1973 and took a position at Yale in 1984. Ullu will receive her award in April during the Experimental Biology 2012 conference in San Diego, where she will deliver the award lecture. The award consists of \$35,000 for use by the recipient's research laboratory, a plaque, and travel expenses for the recipient to attend and speak at the ASBMB annual meeting.

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Student health project offers blood screening

Yale students provide tests, referrals, and advice on handling high blood pressure and blood glucose.

On a cold Saturday morning in January, dozens of people gathered in the basement of the Episcopal Church of St. Paul and St. James, near New Haven's Wooster Square. They came for warmth, companionship, free clothing, and the weekly food pantry run by Loaves and Fishes.

Some also came for free blood pressure and blood glucose screenings provided by Yale students in the health professions. Teams from the School of Medicine, the School of Nursing, and the School of Public Health have been coming to the church for about 10 years as part of the Neighborhood Health Project (NHP). The mission of the NHP is simple—under the tutelage of volunteer physicians, the

students offer screenings and advice about nutrition and exercise. “A lot of our patients have high blood sugar and high blood pressure,” said Sarah Aspinwall, a public health student who's one of four clinic coordinators. “A lot of that is a diet and exercise issue.” Last year the clinic also gave free flu shots to almost 100 people, with vaccine provided by New Haven's health department.

The screenings are the easy part. If the tests reveal a problem, the students refer their patients to a source of free or low-cost health care in New Haven. That's the hard part—many of their patients are unemployed or have limited resources.

One of the patients that morning was 36 years old and recently arrived from Mexico. He hadn't worked in two weeks; before that he had worked intermittently in remodeling. He was worried about his frequent urination and recent weight loss. Carrie A. Redlich, M.D. '82, HS '86, FW '87, M.P.H. '88, professor of medicine (occupational medicine), and this week's preceptor, had questions for the patient: When was the last time you saw a doctor? How much weight have you lost? Why are your pants so loose? Does anyone in your family have diabetes?

First-year physician associate student Lauren Monoxelos had already

done the screenings—the patient's results were off the charts. Jessica Wang, a second-year medical student and one of the clinic coordinators, repeated the tests. Still off the charts. There's only so much the staff can do at a screening clinic, so Redlich made an appointment for the patient at HAVEN, a student-run free clinic on Grand Avenue.

This case offered a lesson beyond the mechanics of strapping a blood pressure cuff on a patient's arm. “For me one of the biggest shockers in terms of interfacing with the medical system has been that when you're studying it, you think the low-income population will just sign up for Medicaid and they'll get care,” said Danielle Correia, a second-year public health student and clinic coordinator. “It seems very simple on paper, but when you're actually in that context you realize the sheer complications of what signing up for Medicaid involves. What if they're just above the poverty line but still very low-income?”

Then there are the lessons in bedside manner. “The thing that we sometimes underestimate is how important it is to get comfortable with patients,” said NHP faculty advisor Jeffrey R. Bender, M.D., HS '83, the Robert I. Levy Professor of Medicine (Cardiology) and professor of immunobiology. “This is a great way for students to start getting a sense of how to talk to people, make them immediately comfortable, and engender trust from the outset.”

“It's really rewarding,” said Wang. “We are helping people get access to health care who would otherwise have a very hard time doing so.”

—John Curtis



JOHN CURTIS

Maureen Wright, a student pursuing dual degrees in public health and the Physician Associate Program, took a patient's blood pressure at the Neighborhood Health Project in January. Students in medicine, nursing, public health, and the PA program also do blood glucose screenings and offer advice about diet and exercise.

Salons bring faculty and students together for wine, books, and conversation

A few days after their return from winter recess, 10 second-year students piled onto a bus in front of the Sterling Hall of Medicine for the 20-minute trip to the Guilford home of Erol Fikrig, M.D., Waldemar Von Zedtwitz Professor of Medicine, Howard Hughes Medical Institute investigator, and professor of epidemiology and public health and of microbial pathogenesis; and of Margaret Fikrig, M.D., assistant professor of medicine. Both specialize in infectious diseases. They were joined by Gerald Friedland, M.D., former director of the AIDS Program at Yale and professor of medicine (AIDS) and of epidemiology (microbial diseases). Friedland has served on the front lines of three epidemics—HIV/AIDS in New York City, HIV/AIDS in South Africa, and extensively drug-resistant tuberculosis in South Africa.

As the group sipped wine and beer in the Fikrigs' living room, the talk turned to the evening's theme—*The Plague*, Albert Camus' 1947 novel about an outbreak of bubonic plague in an Algerian seaport.

The literary salon was the second in a series of four. In December Thomas P. Duffy, M.D., professor of medicine (hematology) led first-year students in a discussion of Rebecca Skloot's history of HeLa cells used widely in medical research, *The Immortal Life of Henrietta Lacks*. In January Warren A. Andiman, M.D., FW '77, professor of pediatrics (infectious diseases) and of epidemiology (microbial diseases), hosted a discussion of Steven Johnson's *The Ghost Map*—the story of John Snow, a pioneer

epidemiologist who traced the source of a cholera epidemic in London in 1854. Michael L. Schwartz, Ph.D., assistant dean for curriculum and associate professor of neurobiology, concluded the series in February with a discussion of Oliver Sacks' *The Man Who Mistook His Wife for a Hat*.

The salons came out of a discussion among faculty members about the relationship between literature and medicine. "Somebody said something and a light bulb went off," said Nancy Angoff, M.P.H. '81, M.D. '90, HS '93, associate dean for student affairs. "We started thinking about books that fit with certain courses. We started thinking biochemistry, we started thinking anatomy, we started thinking cell bio. We put together a committee of students and faculty and came up with these choices." Another impetus was a program launched this academic year—the medical school provided iPads to all students—which allows students to receive free electronic versions of the books.

First- and second-year students were invited to sign up for the salons—the dual goals were to integrate the humanities into students' medical education and to provide a relaxed and informal way for students and faculty to interact.

That night at the Fikrigs' home, Friedland led the discussion of *The Plague*. "This is about death and dying, and the choices that we make at personal, professional, and community levels," Friedland said. "To me it has been a textbook of the HIV/AIDS epidemic, better than any journal article I could read."

One student, Rebecca Vitale, said afterward that the discussion provided a link between the book and modern epidemics. "It talks about the medical profession in the way that it functions in a time of crisis," she said. "That is a piece of medicine that you never talk about."

At the final session a few weeks later at Schwartz's home in Guilford, the discussion veered from the Sacks book to discussions of neurology and to lessons from the accumulated wisdom of



JOHN CURTIS (2)

TOP Gerald Friedland, who observed the HIV/AIDS epidemic firsthand, led the discussion of *The Plague*.

BOTTOM In February Michael Schwartz (left) hosted a discussion of *The Man Who Mistook His Wife for a Hat* with first-year students and neurology professors David Greer and Serena Spudich.

the faculty present. Schwartz and the students were joined by David M. Greer, M.D., vice chair of neurology and the inaugural Dr. Harry M. Zimmerman and Dr. Nicholas and Viola Spinelli Associate Professor of Neurology, and Serena Spudich, M.D., associate professor of neurology.

"Could this book have been written now?" first-year Amanda Wallace asked of the book, written in 1985.

"We thought this is the way medicine was at the time," answered Spudich.

"It's a historical piece," added Greer. "We have treatments now. Now we have a ton of stuff we can do. I don't think you could write this now."

—J.C.

A neurologist inspired by his patients

William Gaillard frees his pediatric patients from debilitating or life-threatening conditions.

When Irving S. Cooper, M.D., was perfecting the stereotactic cryosurgery to treat Parkinson disease in the late 1950s, William D. Gaillard, M.D. '85, was spending summers down the block in Tannersville, N.Y. Developer of the first surgical procedures for Parkinson disease, a pioneer in cryosurgery, stereotactic surgery, and functional neurosurgery, as well as a close family friend, Cooper invited Gaillard to spend a summer during college working with him.

"He was bright and innovative, as well-versed in literature as he was in medicine. My interest in neuroscience stems from his influence," said Gaillard,

who chose pediatric neurology instead of surgery. Gaillard, chief of the Division of Epilepsy, Neurophysiology, and Critical Care Neurology at Children's National Medical Center in Washington, D.C., felt surgery wouldn't allow time for a family, which now includes his 19-year-old son, 16-year-old daughter, and his wife, Adelaide S. Robb, M.D., a principal investigator at Children's National Medical Center. Gaillard proudly describes Robb as "the best pediatric psychopharmacologist east of the Mississippi River. And west."

Gaillard's work, like Cooper's, helps free patients from debilitating or life-threatening neurological conditions. As director of the comprehensive pediatric epilepsy program at Children's National, director of the Intellectual and Developmental Disabilities Research Center Imaging Core, associate director of the Center for Neuroscience Research at Children's Research Institute, and professor of neurology at George Washington and Georgetown universities, Gaillard focuses on difficult-to-control seizures.

In a field that can take a heavy emotional toll, Gaillard draws inspiration from his patients and their parents. The pediatric neurologist tells the story of a 13-year-old patient

with Rasmussen encephalitis, a rare inflammation of one hemisphere of the brain that causes severe seizures, cognitive disabilities, paralysis on one side of the body, and possibly death. If medications don't control the seizures, the only cure is removal of the affected hemisphere of the brain. Typically surgery is not recommended if it will affect movement, memory, or language—functions Gaillard describes as "essential to being human." But even after falling into a coma, the girl was seizing uncontrollably.

"We didn't have any options if we wished to save her life," Gaillard said. So he recommended removal of the left hemisphere of the young girl's brain.

The surgery cured her seizures—but as expected, she couldn't speak or understand. She was depressed, using a wheelchair, and taking numerous medications. A year after surgery, during which Gaillard managed the treatment of a movement disorder the surgery had caused, the once-bright and outgoing girl could speak only one word. "Six months later," Gaillard said, trying to control his emotion, "she walked into my office and said, 'Hello, Dr. Gaillard.'"

Still Gaillard's patient, the young woman now speaks and walks and is back in school; she no longer takes either seizure medications or anti-depressants. Gaillard gives all the credit to the patient and her mother, who encouraged her daughter when

William Gaillard treats pediatric patients who have seizures that are difficult to control. His imaging research allows physicians to determine, noninvasively, whether seizures are located in the areas of the brain that control language.



BILL JENNE

even the girl's schoolteachers said they anticipated no further improvement. She worked tirelessly for her daughter," he said.

Due in part to Gaillard's imaging research, physicians can now determine noninvasively whether seizures are located in the areas of the brain that control language. Among the more than 100 studies Gaillard has led or co-authored, many in collaboration with the National Institutes of Health, he is most excited about his research on using functional magnetic resonance imaging as a replacement for invasive methods of brain mapping. Imaging can reveal which portions of a patient's brain control language to determine whether surgery is a viable option to cure seizures.

Gaillard is quick to explain that he chose pediatrics because "it's more fun." He admires pediatricians' willingness "to play in the sandbox" and "laugh at themselves." For Gaillard, the ability to laugh at himself comes with the ability to "know what you don't know."

"If you really want to take care of someone, it's best if you work closely with others with the skill sets you don't have," he said. Gaillard's own playfulness, not to mention school spirit, is apparent in his bulldog-printed bowtie and e-mails occasionally signed "Boola Boola."

Drawn to medicine by an aunt who was forbidden to go to medical school because "a lady did not take a man's job," Gaillard pursued neurology after a spring spent at University College London's Institute of Neurology at Queen Square. He credits Laura R. Ment, M.D., associate dean of admissions and professor of pediatrics and of neurology, with encouraging his interest in pediatrics and child neurology, and Richard H. Mattson, M.D., professor emeritus of neurology, with encouraging his interest in epilepsy.

"What's really rewarding is to try to help a child have a normal life," Gaillard said.

—*Sonya Collins*

An alumnus' journey: doctor, inventor, and a founder of the UCSD medical school

When Robert Hamburger, M.D. '51, HS '54, was a newly minted University of North Carolina graduate, he planned to become a journalist. Although his career took a very different path—one that led him to become a physician, inventor, and medical school founder—Hamburger never lost his ear for the telling anecdote or colorful quote.

On the subject of deciding to become a doctor, he said, "I used to baby-sit for our family doctor's two kids. I would sneak into his office to look at his books, mostly to look at the sex pictures, but it left me with a genuine interest in medicine."

On religion: "During my first interview at the medical school, the interviewer asked me about my religion, and I told him I was an atheist. Knowing I'd served in the war (Hamburger was a P-38 pilot during World War II), he said, 'There are no atheists in foxholes.' I told him that was a load of crap; I became an atheist when I saw what human beings do to each other."

And on the death of two of his three daughters from cancer: "It was very tough. I've saved a large number of very sick patients in my career, but I couldn't save my own kids. I have quite a strong ego, but that gave me a good sense of humility."

Hamburger is best-known for discovering the relationship of allergy inheritance and IgE (one of the five immunoglobulins humans have in their bodies) in mothers and infants, inventing a high-efficiency particulate filter to aid children with asthma, and

helping to launch the University of California School of Medicine in La Jolla. He credits his training at Yale, especially studying under the Yale system, for his success on all these fronts. The Yale approach, with its emphasis on research-based medicine in a noncompetitive environment, taught Hamburger the importance of questioning conventional wisdom and insisting on scientific evidence to support one's hunches and beliefs.

"It became my model, the model that I operated on," he said. "I would drive people crazy when I'd say, 'That sounds kind of like hearsay. Is there any evidence to back it up?' But that's how I think; that was my training."

Hamburger applied to the School of Medicine at the urging of his sister Evelyn, who had been accepted by the Yale School of Nursing. Without the support of his wife, Sonia, to whom he's been married for 67 years, he wouldn't have made it through, he said. (Her support when he was missing in action during World War II also helped his parents get through that crisis.) After he completed his residency at Yale and at Strong Memorial Hospital in Rochester, N.Y., he became the chief of pediatrics at Milford Hospital in Connecticut. "I was broke. I owed everybody money, so I worked 16- to 18-hour days, seven days a week, to get out of debt." After four years, Hamburger returned to Yale to become a postdoc in the microbiology department. Six months later, in 1964, he followed his division chief, David M. Bonner, PH.D., to the University of California, San Diego (UCSD). The timing was fortuitous, as UCSD was then launching a medical school and Hamburger was asked to sit on the advisory committee.

(Yale connections to UCSD are strong and deep. Former Dean Gerard N. Burrow, M.D. '58, HS '66, served as dean of the medical school there from 1986 to 1992. Nobel laureate George E. Palade, M.D., left Yale in 1990 to become the first dean of scientific affairs at UCSD. The current dean of



MELISSA JACOBS

Robert Hamburger is best-known for discovering the relationship between allergy inheritance and an immunoglobulin in mothers and infants. He was also a founder of the medical school at the University of California, San Diego.

the medical school at UCSD is David A. Brenner, M.D. '79, HS '82.

Drawing on his experience at Yale, Hamburger recommended the aspects of his Ivy League education he valued most, while rejecting “the stuffiness and formality.” That meant no competition and no grades at the new school. The school should be small, and students should be required to complete a thesis based on original research in order to graduate.

His suggestions were well-received, and Hamburger was encouraged to stay on, first as assistant dean for faculty and curriculum affairs, and later as head of the school's Pediatric Immunology and Allergy Division and as assistant dean of the medical school. He became a professor emeritus in 1990.

Throughout his career Hamburger's work has focused on allergic diseases and their impact on children's health.

In the late 1990s he developed an allergen detector system to help children with asthma sleep more soundly. “Sunbeam bought the rights, but then they went belly up,” he said. “I still have samples of that device in my closet. It was the one effort in my life to try to get rich.”

More successful was his collaboration with Nestlé, the Swiss food and confectionery company, which asked Hamburger to serve on its advisory board to help promote its baby formula. Hamburger said he would participate only if the company helped him spread the word about the benefits of breast feeding, which include later resistance to allergies. “Our message was ‘breast is best, but if you can't nurse or you need to supplement, use Nestlé baby formula.’”

Now well into his retirement, Hamburger has returned to his first vocational love—writing. He and his

granddaughter Toya are collaborating on a collection of short stories that will constitute his autobiography. Tentatively titled *Autobiography: A Long Life in Short Story*, it is about 25 pages long, but promises to grow much longer.

—Jennifer Kaylin

Familiar Faces

Do you have a colleague who is making a difference in medicine or has followed an unusual path since leaving Yale? We'd like to hear about alumni of the School of Medicine; Physician Associate Program; and the medical school's doctoral, fellowship, and residency programs. Drop us a line at ymm@yale.edu or write to Faces, Yale Medicine, 1 Church Street, Suite 300, New Haven, CT 06510.



C. Norman Coleman



Ross Tonkens



Ronald Vender



Gerard Doherty



**Emma Webber
Adam Kaye**



**Philip Butler
Carolyn Goldberg**

1970s

C. Norman Coleman, M.D. '70, received the 2011 Homeland Security Medal, a Samuel J. Heyman Service to America Medal presented annually by the Partnership for Public Service to honor excellence in federal civil service. This medal recognizes federal employees for significant contributions to the nation in activities related to homeland security. Coleman, associate director of the Radiation Research Program at the National Cancer Institute of the NIH, developed a blueprint for dealing with the health consequences of a radiological or nuclear incident.

Harry Romanowitz, M.D. '73, clinical assistant professor in the Department of Pediatrics, received Sacred Heart University's College of Health Professions 2011 Community Partner Award. The award is given in recognition of "exceptional collaboration to further the educational goals and mission of the college." His teaching and mentoring of nurse practitioner and nursing students through the first urgent care pediatric practice in Fairfield County (which he founded in 2007) provides outstanding clinical training for students. Romanowitz served for 20 years as Stamford Hospital's chair of pediatrics and maintains his consultation practice.

Ross Tonkens, M.D. '74, has been appointed head of the American Heart Association's (AHA's) new Science and Technology Accelerator division. He is charged with identifying and vetting potentially "game-changing" scientific innovations aligned with

AHA's core mission—to foster healthier lives free of cardiovascular diseases and stroke—that are insufficiently developed to attract private equity funding, and with accelerating their translation into products that improve real-world cardiovascular outcomes.

Ronald J. Vender, M.D. '77, HS '80, FW '82, chief medical officer of Yale Medical Group and a nationally recognized gastroenterologist specializing in therapeutic endoscopy and inflammatory bowel disease, was appointed vice president of the American College of Gastroenterology (ACG). The mission of the ACG is to advance the medical treatment and scientific study of gastrointestinal disorders.

1980s

Gerard M. Doherty, M.D. '86, has been appointed chair of the Department of Surgery at Boston University School of Medicine and chief of surgery at Boston Medical Center effective January 1. Doherty was previously at the University of Michigan, where he was N.W. Thompson Professor of Surgery, vice chair of the Department of Surgery, and section head of General Surgery. Doherty's clinical focus is endocrine oncology; it comprises diseases of the thyroid, parathyroid, endocrine pancreas, and adrenal glands, as well as the surgical management of multiple endocrine neoplasia syndromes. His research interests include a series of projects to regenerate parathyroid cells for replacement of lost tissue in people who are permanently hypoparathyroid.

1990s

Joshua Broder, M.D. '99, who published *Diagnostic Imaging for the Emergency Physician* (Elsevier 2011), was announced as the 2011 winner of the PROSE Award in Clinical Medicine. The PROSE Awards are the American Publishers Awards for Professional and Scholarly Excellence. Broder is associate professor and residency director in emergency medicine at Duke University Medical Center.

2000s

Jeremy Allen, M.M.Sc., PA-C '07, and **Maria Teresa Trigg, M.M.Sc., PA-C '09**, were married on October 22 in the Great Smoky Mountains of North Carolina. Allen works as a physician associate in emergency medicine and Trigg is in private practice in Connecticut.

Eric Arzubi, M.D. '08, HS '11, received the Resident Physician Community Service Recognition Award (CSRA) from the Association of American Medical Colleges in November. The CSRA is given to one resident around the country each year and recognizes contributions that improve the communities surrounding the resident's training institution. Arzubi, a fellow in adult psychiatry at the School of Medicine, was honored for helping to organize and lead a mental health advocacy coalition in Connecticut, the Children's Committee of the Keep the Promise Coalition. The coalition's primary goal is the expansion and enhancement of school-based mental health services.

Adam H. Kaye, M.D. '09, M.B.A. '09, and **Emma J. Webber** were married in Guilford, Conn., in

September. Among the wedding party were **Christopher Spock, M.D. '09**, and **David Gimbel, M.D. '10**. Kaye is a radiology resident at the Hospital of the University of Pennsylvania. Webber is pursuing a career in environmental public policy.

David LaBorde, M.D. '04, M.B.A., is the co-founder and CEO of Iconic Data, which offers physicians a tool for managing patient data across facilities. Iconic Data was recently selected as a part of the inaugural class of Healthbox, a Sandbox Industries business incubator funded by Blue Cross and Blue Shield. LaBorde spent six years in neurosurgery and previously worked in management consulting at McKinsey & Co. and in health care investment banking at Goldman Sachs and Merrill Lynch.

2010s

Philip Butler, M.D. '10, and **Carolyn Goldberg, M.D. '10**, were married in October in Anguilla in the British West Indies. The couple completed residencies at the University of Wisconsin Hospital and Clinics in Madison—she in plastic and reconstructive surgery, he in diagnostic radiology. In November Butler began a residency in radiology at Brigham and Women's Hospital in Boston.

SEND ALUMNI NEWS TO Claire M. Bessinger, *Yale Medicine*, 1 Church Street, Suite 300, New Haven, CT 06510, or via e-mail to claire.bessinger@yale.edu

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Malcolm Bagshaw, M.D. '50, one of the world's foremost experts in radiation therapy, most notably in developing new applications of radiation therapy for prostate cancer, died on September 18 at home in Palo Alto, Calif., after an extended illness. He was 86. Bagshaw was the former chair of the departments of radiology and radiation oncology at Stanford University School of Medicine. He completed his residency in radiology at the University of Michigan and joined Stanford in 1956. He was appointed head of the Division of Radiation Therapy in 1960 and became chair of the Department of Radiology in 1972. Bagshaw received the 1996 Charles F. Kettering Prize, awarded by the General Motors Cancer Research Foundation, for his role in improving prostate cancer treatment.

John D. Baxter, M.D. '66, HS '68, whose early work in cloning and recombinant protein production provided the basis of the biotechnology industry, died of cancer on October 5 in San Francisco. A native of Lexington, Ky., he was 71. At the time of his death Baxter was director of the Genomic Medicine Program of the Methodist Hospital Research Institute in Houston. By cloning the growth hormone family of genes and through subsequent studies, Baxter made major contributions to the understanding of growth and development, and established a model for advances in developmental biology. That model led to the creation of the first synthetic drug to stimulate growth in children of abnormally short stature and the discovery of drugs to increase milk production in dairy cows. Baxter and a colleague then became the first to show what a nuclear receptor looks like when it is binding to a hormone—a breakthrough that led to new structures in drug design. Baxter was named to the National Academy of Sciences in 2003. He also received an Outstanding Investigator Award from the Howard Hughes Medical Institute.

Harold O. Conn, M.D., FW '53, HS '56, a world-renowned hepatologist, author, and pioneer in the basic understanding and treatment of advanced liver disease, died on October 9 in Pompano Beach, Fla. He was 85. Conn, a 50-year faculty member at the School of Medicine, wrote more than 400 peer-reviewed articles about hepatic encephalopathy. One of Conn's greatest professional accomplishments was *The Histopathology of the Liver*, published in 1993, which he wrote with Gerald Klatskin, M.D. It was his last major project until he contracted normal-pressure hydrocephalus (NPH). Erroneously diagnosed for 10 years as Parkinson disease, NPH robbed him of his ability to walk or think clearly until the correct diagnosis was made. Following a remarkable remission after brain surgery at age 78, Conn became a spokesperson for NPH awareness.

We have also received word of the passing of the following alumni and faculty:

Mary North Allen, MED '45, a photographer, died on November 26 at her home in Madison, Wis. Allen was 92. After her graduation from Mills College in 1941, she attended Yale School of Medicine for one year.

Carl E. Andrews, M.D. '44, died on September 12 in Fort Pierce, Fla. He was 91. Andrews was a retired general surgeon who had practiced in West Palm Beach for 33 years.

Graeme C. Baker, M.D., HS '76, a plastic surgeon, died on October 2 in Erie, Pa. He was 73.

Dennis P. Bekeny, M.D., HS '72, of Hamden, Conn., died on October 6 at Smilow Cancer Hospital at Yale after a brief illness. Bekeny was a pediatrician in the New Haven area for 36 years.

Donald Smythe Childs Jr., M.D. '42, a retired radiologist, died on December 10 in Rochester, Minn. He was 95.

George M. Goza Jr., M.D., HS '56, died at home on October 19 in Rice Lake, Wis. A retired internist and cardiologist, Goza was 85.

Robert H. Groves Sr., M.D. '56, died on October 31 in Rochester, Mich. He was 81.

James W. Innes, M.D., HS '63, FW '64, died on August 29 in Riverside, Conn. He was 79. Innes practiced internal medicine and gastroenterology.

William H.O. Kiekhofer, M.D. '51, a retired associate professor of obstetrics and gynecology at the University of Wisconsin Medical School, died on October 13 in Providence, R.I. He was 89.

Ruth H. Kotler, PA-C '88, a neurosurgical physician associate at the University of Connecticut Medical Center, died at home in Avon, Conn. on November 5 of breast cancer. She was 47.

Cheryl E. Lemmons, M.D., HS '87, a surgeon and geriatric psychiatrist, died in Onset, Mass., on August 6 after a short illness.

Francis B. Maraist, M.D., HS '55, a retired general surgeon, died on November 1 in Tequesta, Fla. He was 85.

Robert N. Margolis, M.D., HS '65, associate clinical professor of orthopaedics and rehabilitation, died in Woodbridge, Conn., on September 21. He was 78. Margolis served as associate chief of orthopaedics at the Hospital of Saint Raphael, chief of orthopaedics at the VA Connecticut Healthcare System in West Haven.

Nessan McCann, M.D., HS '66, died on September 14 in St. Augustine, Fla. He was 88.

K. Alvin Merendino, M.D. '40, PH.D., a retired professor of surgery at the University of Washington Medical Center, died on September 10 in Seattle. He was 96. Merendino performed the first open-heart surgery on the West Coast and helped

establish a renal transplantation program in Seattle.

Richard Neubauer, M.D. '76, died on October 31 at his home in Stuckagain, Alaska, from complications of primary amyloidosis. Neubauer was 61. Born in Queens, N.Y., he served in the Indian Health Service in Wyoming before moving to Alaska.

John A. Ogden, M.D. '68, HS '73, died in Atlanta on August 31. He was 68. Ogden served as chair of orthopaedics at the School of Medicine from 1978 to 1983 and later as clinical professor of orthopaedics at Emory University.

Thomas R. Pellegrino, M.PHIL. '71, M.D., HS '77, died at home in Hampton Roads, Va., on November 17 after a short illness. At the time of his death, Pellegrino was associate dean for education at Eastern Virginia Medical School.

Jeffrey Robbins, M.D., HS '68, a retired otolaryngologist, died on July 13 at his home in Bristol, Tenn. He was 69.

Ben A. Shaver Jr., M.D. '56, a retired pediatrician, died on November 23 in Potomac, Md. He was 81.

Don H. Smith, M.D. '70, a prison psychiatrist, died on October 12 in Port Washington, Wis. He was 66. Smith was a junior research fellow in the Yale Arbovirus Research Unit during his years at the School of Medicine.

Martin B. Vita, M.D. '50, a retired pediatrician, died on September 18 in New York City. He was 83.

Douglas A. Wegner, M.D., HS '94, a hand surgeon, died suddenly of a heart attack on August 5 in Tucson, Ariz., while running in Sabino

SEND OBITUARY NOTICES TO Claire M. Bessinger, *Yale Medicine*, 1 Church Street, Suite 300, New Haven, CT 06510, or via e-mail to claire.bessinger@yale.edu

Second-years save the Yale system!

Egregious violations of the Yale system—mandatory class attendance and exams—drive a student to the breaking point in the Class of 2014’s Second Year Show, *The iPocalypse*, presented in February. The heroine, played by Juliet Fraser, finds her dreams of a career in neurosurgery thwarted on Match Day. “Podiatry!?” she screams. All ends well, however, when students put an end to a scheme by an evil consultant played by Samantha Wang (who co-directed the show with Conor Grady). Left to right, Alex Kula, Kelsey Loeliger, Grady, and Fraser appear in a scene from the show.

