

# BROWN JOURNAL OF MEDICINE

FALL 2006

## MARRIED TO MEDICINE

How MD Couples  
Make It Work





## From the Editor

YEARS AGO I LOST TOUCH WITH A WOMAN I KNEW AND liked when our families moved—hers to England, mine to the States. We'd both lived in Paris for a long time, but had only recently met as a result of one of those weird Rhode Island connections that only half take you by surprise, even when you're 3,000 miles away.

The next time I heard from her was at home in Providence a couple of years later, when she called me out of the blue to say they had settled less than an hour away, in Massachusetts. What surprised me even more was the story of what had brought them there. Shortly after we had said goodbye, the older of her two very young boys began to show severe developmental problems, eventually losing both of his languages as well as his acquired social skills. He was diagnosed with autism. The family had come here in large part because of the special care available—including in the public school system.

It seemed uncommon at the time, but in the intervening years the topic of autism has become almost as ubiquitous as HIV/AIDS or cancer. The parents, kids, clinicians, and caregivers in our feature on autism are all admirable in their own way for the role they play in elucidating the mysteries of this disorder and in refining our understanding of and sensitivity to it.

So what's that got to do with diabetes? Not much—except that diabetes is becoming more and more a disease that affects children, which means that how we deal with it now will undeniably shape the future. Lucky for us, physician-scientists like Robert Smith and his colleagues are focused on finding the causes, devising the cures, and treating those affected.



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photographed by Scott Kingsley

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# BROWN MEDICINE

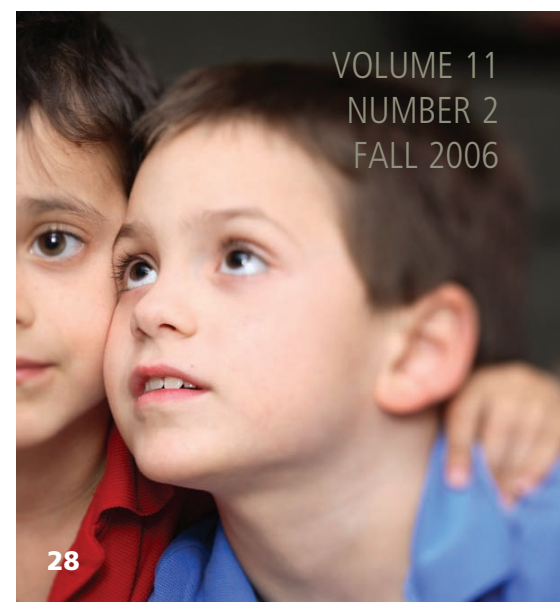
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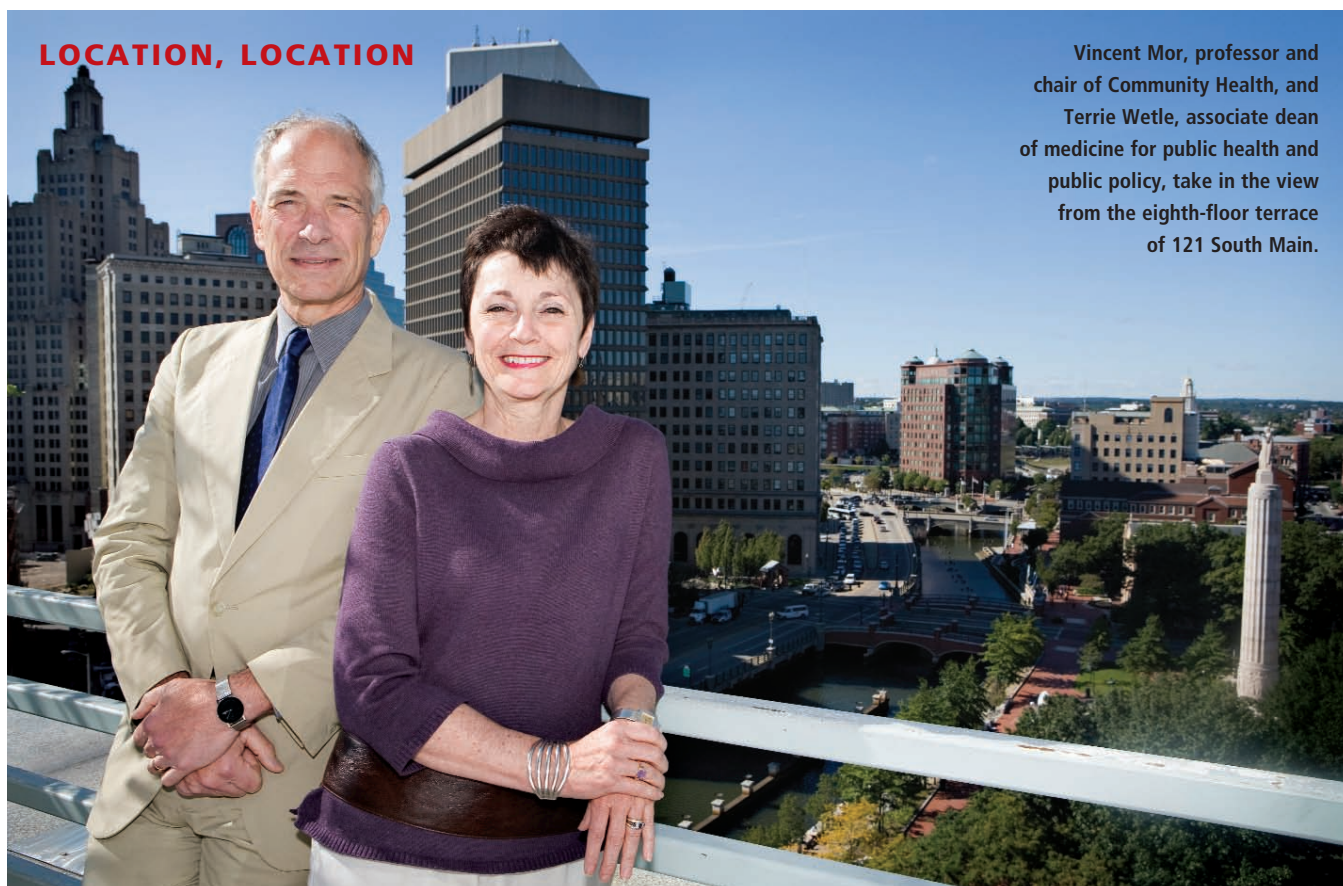


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# Vitals

## LOCATION, LOCATION



Vincent Mor, professor and chair of Community Health, and Terrie Wetle, associate dean of medicine for public health and public policy, take in the view from the eighth-floor terrace of 121 South Main.

# On Top of the World

OVER THE COURSE OF SEVERAL WEEKS last summer, the Program in Public Health began moving into its new home at 121 South Main Street. The building will house most of the Program's nine public health centers as well as the Department of Community Health, with room to spare for future expansion.

The move is critical to accommodating the Program's growth. Over the past decade, public health has assumed increasing importance for the nation and the world, and research in the field has experienced steady growth at Brown. External funding of public health faculty has increased substantially, too, fueled by basic sci-

entific findings and a growing need for translational research and effective interventions. In addition, four new tenure-track faculty have been hired to date (with plans to reach 27) to support new multidisciplinary research initiatives and consistently growing numbers of undergraduate and graduate students in public health.

Purchased last year by the University, the building's 11 stories and 126,000 square feet of net usable space contain offices, computer labs, research space, classrooms, a lecture hall, and meeting areas. Because much of the building is occupied and existing lease contracts are still in force, the move is

being phased in as space becomes available: approximately 57,000 square feet are occupied, and up to 90,000 square feet (or approximately 75 percent of the building) will be by 2010. The ground floor will continue to support retail activities.

Terrie "Fox" Wetle, PhD, associate dean for public health and public policy, says that the new location, which is close to the Department of Health, community agencies, and the Jewelry District, facilitates collaboration, adding that "the four-block uphill walk to the Green is great exercise—an added public health benefit!"

— SARAH BALDWIN-BENEICH

LUCAS FOGLIA



FINDINGS

## Death of a Parasite

AS MUCH AS 65 PERCENT OF THE world's population may be infected by *Toxoplasma gondii*, a crafty one-celled parasite often carried by cats. But it rarely causes illness in humans because the immune system keeps it in check—and because it can, in a clever way, avoid detection.

When *Toxoplasma gondii* is found out, though, the immune system kills it through a grisly process, according to research led by George Yap, assistant professor of medical science in the Department of Molecular Microbiology and Immunology. The intracellular parasite is stripped, surrounded and devoured through a strange self-eating process cells use to remove and reuse old or damaged parts.

The study appeared in the September *Journal of Experimental Medicine* and was featured as an “Editors Choice” in *Science* and as a “Research Focus” in *Trends in Immunology*. The research is the first to detail how *Toxoplasma gondii* are killed off by the immune system.

It's also the first to show that para-

sites can be disposed of through autophagy, a cellular recycling process that allows for healthy cell growth and development and appears to suppress, or in some cases aid, cancerous tumors.

“It's just become clear in the last two years that autophagy can kill viruses and bacteria ...,” says Yap. “Now we know that the process can destroy parasites, too.”

*Toxoplasma gondii* belongs to a stealthy—and therefore successful—class of parasites that includes the malaria parasite. On entering a cell, the parasite builds a “safe house.” The membrane sac, or vacuole, lacks the receptors that would allow lysosomes, the cell's gobbling garbage collectors, to attach themselves and start feasting.

So how does the immune system destroy such a cunning opponent?

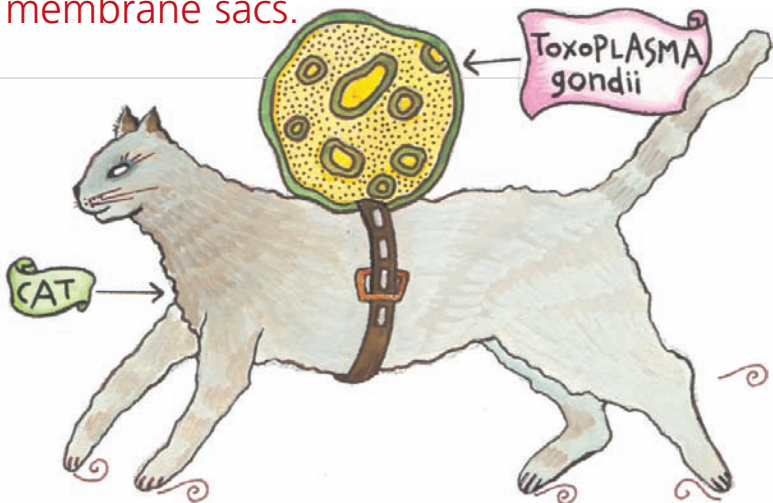
To find out, researchers activated macrophages (white blood cells triggered by the immune system) and inserted the parasites. They found that interferons, proteins produced by cells of the immune system, switch on a gene called IGTP. While its precise role is a mystery, Yap's team (which includes graduate students Yun Ling and Michael Shaw) found that activation of IGTP is critical, prompting the

macrophage to form finger-like appendages that feel out the parasite inside its safe house. These “fingers” then pull at the membrane of the house until it disintegrates, exposing the parasite.

Next, the macrophage peels off the parasite's membrane and autophagy kicks in. The naked bug, spilling its innards, is enveloped in two membrane sacs, the outer sac containing the receptors that lysosomes can attach to. Once the lysosomes arrive, they consume the parasite's remains.

“Now that we better understand this destructive process,” Yap says, “the question is: Can you induce it with a drug? If so, that drug could provide protection from all sorts of harmful pathogens.” — WENDY Y. LAWTON

The naked bug, spilling its innards, is enveloped in two membrane sacs.



JESSICA DEANE ROSNER

STATS

### Anatomy of the Class of 2010

STUDENT BODY

92 total	
Female	50%
Male	50%

AGE RANGE UPON MATRICULATION

21-37 years

ADMISSION ROUTES

PLME	48
Standard	33
MD/PhD	2
Postbaccalaureate	6
EIP	3

COLLEGE MAJORS

Humanities	44%
Science	56%
• Physical and life sciences	49%
• Engineering, math, or computer science	7%



## Vitals

### PUNCHLINE

#### Make Mine Decaf

A CUP OF COFFEE MAY CAUSE A heart attack in some people within an hour of drinking it, according to a study reported in *Epidemiology*. Ana Baylin, assistant professor of community health at Brown, and colleagues at Harvard School of Public Health surveyed participants about their coffee consumption in the hours and days before their heart attack. They found that the moderate coffee drinkers, by having a cup of coffee, increased their risk of heart attack by 60 percent. There was little effect among heavy coffee drinkers, but light coffee drinkers increased their risk by more than four times—perhaps because they are less acclimated to the effects of caffeine. Patients with three or more risk factors for coronary heart disease more than doubled their risk. “People at high risk for a heart attack who are occasional or regular coffee drinkers might consider quitting coffee altogether,” Baylin suggests.



and sent helpful tips via email, they encouraged participants to design their own programs according to personal preferences.

“We didn’t tell people exactly what to do,” Kumar explains. “It was up to each team to figure out what worked best for them. In the end it was as if we had hundreds of different weight-loss and exercise programs going on, each tailored to the needs and interests of individuals.” And many took full advantage of that freedom. “People were so creative,” Kumar says. “One group organized a tag-team event at work where one member would walk around the building for 15 minutes and then tag another team member to do the next 15 minute shift. So at every point in the day, there was one team member walking and accumulating exercise time.”

Kumar says such camaraderie within teams was a key factor in the Shape Up RI strategy. In his first year of the Med School’s new Doctoring course, which offers students their first clinical



Kumar at opening ceremony with Channel 12 news anchor Karen Adams and Team Faith

divide to tackle a common adversary: the obesity epidemic. Lawmakers like Congressman Patrick Kennedy and Rhode Island Governor Donald Carcieri, along with community leaders Dean Eli Y. Adashi and Rhode Island Hospital CEO Joe Amaral MD’81, lent support to Shape Up Rhode Island, a health campaign founded and chaired by Kumar. “It was an easy issue for leaders to support,” he says. “Obesity is the number one public health challenge that we face as a nation.”

From March through June 2006, Shape Up RI inspired more than 200 teams of family members, friends, and co-workers from across the state to compete for the biggest drop in pounds and highest increase in hours of physical activity. But by the competition’s end, all 1,738 participants had won, losing a total of 5,911 pounds and logging 69,132 hours of exercise. The winning teams were honored at a June awards ceremony.

Much of the program’s success can be credited to its hands-off approach. While staffers monitored team progress

**Kumar was struck by how isolated patients could be in their struggle to lose weight.**

experiences with local physicians in office settings, Kumar saw patients at a family medicine practice and was struck by how isolated they could be from others in their struggle to get to a healthy weight. “But with Shape Up,” he says, “participants are not alone. The peer support and group motivation proved very powerful in helping people to change their behaviors and reach their personal goals.”

— JUMOKE AKINROLABU

ISTOCKPHOTO: COURTESY KUMAR

### INITIATIVES

#### Weighty Matters

RAJIV KUMAR ’05 MD’09 COULD TEACH the folks on Capitol Hill a thing or two about diplomacy. Recently the second-year student brought together leaders from opposite ends of the political



## UPDATE

### Breakout Role

WHEN DR. SUSAN CU-UVIN ESTABLISHED the HIV-Menopause Clinic at The Miriam Hospital, she hoped not only to help her patients with HIV who, thanks to antiretroviral drugs, are now living well into middle age, but also to gather data on the little-understood co-existence of HIV and menopause. Now her work has been recognized with the inaugural Health Breakthrough Award from *Ladies' Home Journal*.

The award recognizes leading medical professionals who are making life-saving and life-enhancing discoveries



Susan Cu-Uvin

in research, diagnostics and treatment—with results that have significantly helped women and families. Cu-Uvin was honored for establishing the HIV-Menopause Clinic, the first in the nation specifically devoted to the population of menopausal women with HIV/AIDS (see *Brown Medicine*, Spring 2004).

Cu-Uvin, a professor of obstetrics and gynecology and medicine and director of The Immunology Center at The Miriam, was selected from a candidate list of nearly 100 accomplished professionals. She was honored along with

**Cu-Uvin was honored for establishing the nation's first clinic devoted to menopausal women with HIV/AIDS.**

## MILESTONE

### Family Reunion

ON SEPTEMBER 8, 300 PEOPLE GATHERED AT PROVIDENCE'S BILTMORE Hotel to celebrate three decades of academic family medicine at Brown and in Rhode Island. The gala event was also the occasion of the inaugural Elise M. Coletta, MD, memorial address, delivered by President Ruth Simmons.

Among those joining the celebration were Governor Donald Carcieri, Congressmen Patrick Kennedy and James Langevin, deans emeriti David Greer and Stanley Aronson, and Vincent Hunt, founding chair of the Department of Family Medicine. Jeffrey Borkan, current chair of the department and of the Rhode Island Academy of Family Practice, planned the event to coincide with both the family medicine residency program's 30th anniversary and the RIAFP's annual conference. Borkan praised Memorial Hospital's longstanding support of the program, whose 350 graduates account for nearly 70 percent of the family physicians in Rhode Island.

To learn more, go to <http://bms.brown.edu/media/familymedicine30>.



Mary Kay Hunt,  
Vincent Hunt, and  
Arthur Frazzano

six other doctors and researchers at the Health Breakthrough Awards Luncheon in New York City on August 2, hosted by *Ladies' Home Journal*, with special presenters including actresses Sally Field and Andie MacDowell and news anchor Ann Curry. The honorees were also featured in the September issue of the magazine.

With her staff at the clinic, Cu-Uvin hopes to gain insight into several unanswered questions, including whether menopause and HIV work together to hasten bone loss, if menopause occurs earlier or later in HIV-positive women, and if HIV-positive menopausal women place their partners at a higher risk for HIV infection through sexual contact. Determining what effect hormone replacement therapy has on HIV-positive women also remains to be seen.

— KRIS CAMBRA



## Vitals

### Q+A

## Helping Women Faculty Arrive and Thrive

WHEN PAMELA O'NEIL PHD'91 TALKS about advancing the careers of women in science, she knows of what she speaks. O'Neil was on the faculty of the University of New Orleans for 15 years after receiving her PhD from the Department of Ecology and Evolutionary Biology.

Now associate provost for policy and planning at Brown, O'Neil is PI on a new \$3.3 million grant from the National Science Foundation's ADVANCE program aimed at increasing the representation and advancement of women in science and engineering academic careers. The grant announcement coincided with a report from a National Academies panel, of which President Ruth Simmons was a member, that found women are under-represented in academic leadership positions in science and mathematics not because they are innately less capable than men, but because of biases, discrimination, and institutional structures.

"For women scientists it's not a comfortable thing to talk about," O'Neil says. "Women scientists want to do science. As an administrator, I feel strongly that we need to tackle the institutional problems that keep women from being successful."

*Brown Medicine* spoke with Associate Provost O'Neil about the grant and what it means for Brown.

### What is an ADVANCE Institutional Transformation Award?

THE IDEA IS TO GIVE INSTITUTIONS awards so they can transform themselves into places where women are able to succeed at the highest level. The National Academies report showed that even though there are a lot of women in the pipeline, there aren't as many at the full professor level. Because at Brown



Pamela O'Neil

we have a president who was already dedicated to the recruitment of women, we decided to work a level higher and concentrate on retention.

### What is the focus of the grant?

FACULTY DEVELOPMENT PROGRAMS—but not for women, because all faculty need help in order to be successful as they can be. This fits in with the Plan for Academic Enrichment and the idea that we want all Brown faculty to have the opportunity to be superstars. If we have fair, transparent faculty development programs, then women will succeed under that sort of system.

### What do you mean by "transparent?"

SOMETIMES WOMEN FEEL THAT THEY don't have access to the same resources that male faculty do. Often, that's because access is informal. That's where you have the lack of transparency. Women feel like if they ask for something it's going to be seen as a special favor, and they don't want to be seen as succeeding because of special favors. Resources should be available in a transparent way. Even if the effect in each case is small, the cumulative effect over a career can be substantial.

### Can you describe a few of the specific initiatives funded by the grant?

THERE ARE TWO LEVELS OF MENTORING, for instance. One will work with

department chairs to develop a mentoring program within their department to help junior faculty meet the challenge of getting money from a national funding agency. Another will provide assistant professors with a mentor outside of their department if they would like one. Often because the people in your department will be the ones voting on you at tenure time, there's a reluctance to voice concerns with them.

The grant will also provide funds for career development awards that will help faculty network with colleagues across the country and develop new collaborations.

For women who want a leadership role in an administrative position, we'd like to provide an opportunity for them to get experience. We're not trying to make women who are scientists become administrators. We want there to be two very distinct leadership opportunities, because we recognize that the best way for women to be leaders is to be good scientists first.

### The physical sciences saw a jump in women faculty hires. How are the life sciences doing?

THE LIFE SCIENCES HAVE BEEN FLAT. IF we just stay at 30 percent, is that really good enough when the pipeline suggests that we could be at 40 percent?

— K. C.

DONALD TETTO



## FINDINGS

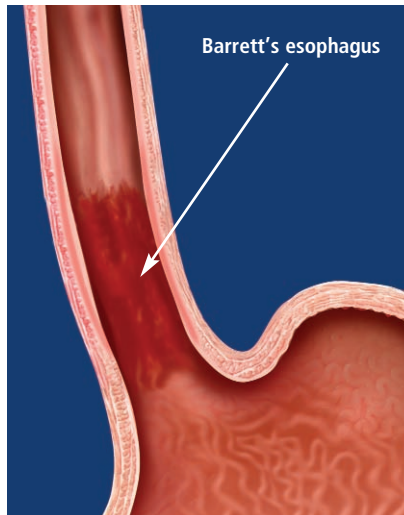
### Acid Test

YOU'VE HEARD THE COMMERCIALS: "the acid churning up," "the little purple pill." Everywhere you turn, there's a remedy for gastroesophageal reflux disease (GERD).

And rightly so. GERD is more than just a little discomfort from eating a spicy burrito. If left untreated, it can lead to a condition called Barrett's esophagus, which is often a precursor to esophageal cancer.

Now, researchers at Brown and Rhode Island Hospital have outlined the signaling pathway from cellular damage by acid to the progression of esophageal cancer. Their work was published in the *Journal of Biological Chemistry*.

Looking at human cancer cells and biopsies from patients with Barrett's esophagus, the researchers found that the enzyme NOX5-S is affected by exposure to acid and that it produces stress on cells, activating genes that



of reactive oxygen species, increasing cell growth and decreasing cell death—optimal conditions for cancer to develop.

"The role of acid is controversial ... Now that we have a better understanding of the signaling pathway, we can

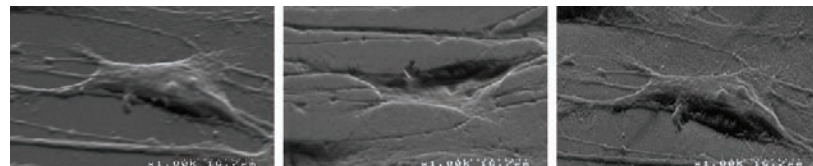
possibly identify who is at risk of developing cancer by determining the levels of this enzyme," says senior author Weibiao Cao, an assistant professor of medicine and surgery and a researcher at the Liver Research Center, Rhode Island Hospital.

Now that the sequence of events is understood, researchers can attempt to slow down or even block the progression of cancer by blocking different steps, providing therapeutic value to patients.

And that's timely news, since incidences of esophageal cancer related to Barrett's esophagus have increased over the past three decades at a rate exceeding that of any other cancer in the past 10 years. Patients have a poor prognosis, with a median survival of less than 18 months after diagnosis, and the five-year survival rate is less than 20 percent after surgery on operable tumors.

— K. C.

## PUNCHLINE



### Genuine Fakes

DIANE HOFFMAN-KIM, ASSISTANT PROFESSOR IN THE DEPARTMENT OF Molecular Pharmacology, Physiology and Biotechnology and the Division of Engineering, and her team have cast plastic replicas of real cells through a novel two-part molding process. They describe their findings in *Langmuir*, a journal of the American Chemical Society. The cells used in the experiments were Schwann cells, which protect peripheral nerves by wrapping around their axons to create insulating myelin sheaths; they also direct axon growth during cell development and repair. In addition to being used in laboratories to help scientists understand how these cells sustain and direct nerve growth, the fakes could also eventually be used in hospitals to help regenerate nerves.

Jan Bruder, a student in the Artificial Organs, Biomaterials and Cellular Technology graduate program, is the lead author. Other research team members are Michael Harrison, another graduate student in the program, and Nicholas Monu '06 MD'10.

— W.Y.L.

"We can possibly identify who is at risk of developing cancer by determining the levels of [the NOX5-S] enzyme."

lead to DNA damage. NOX5-S is significantly higher in Barrett's esophageal tissues. Acid exposure leads to an increase in calcium in Barrett's esophageal cancer cells, thus activating a cAMP response element binding protein. This, in turn, causes the activation of NOX5-S and overproduction



## Vitals



### FINDINGS

#### Mirror, Mirror

THE BROODING TEENAGER IS AS WELL known to parents and caregivers as the “terrible twos” of infancy. But children admitted to the inpatient adolescent psychiatric unit at Bradley Hospital are in the sort of pain that goes beyond teen angst.

“These children want to hurt themselves,” says Jennifer Dyl, clinical assistant professor of psychiatry and human behavior and supervising psychiatrist at the unit. “Many come in after attempting suicide.” It is from this group that Dyl and a team of researchers pulled the sample for the largest-ever clinical study of Body Dysmorphic Disorder (BDD) in adolescents.

BDD is a condition in which one is tormented by some perceived flaw in his or her appearance. Victims sometimes spend hours a day engaging in a number of compulsive behaviors to right the imagined wrong, from skin picking and mirror checking to, in extreme cases, self-mutilation. BDD can drive the afflicted into self-imposed isolation and to suicidal ideation. Though most adult sufferers

trace their struggle with the condition back to their teens, little research has been conducted among adolescents.

Dyl’s team administered the Body Dysmorphic Disorder Questionnaire (BDDQ), a tool developed for use in adults by study co-author Katharine Phillips, professor of psychiatry and human behavior and director of the Body Dysmorphic Disorder and Body Image Program at Butler Hospital. “Questions about BDD aren’t typically part of a routine [pediatric] psychiatric work-up,” Dyl says. “This was the first time the BDDQ was used with children.”

The findings, published in June in the *Journal of Psychiatry and Human Development*, showed that many of the teens had undiagnosed BDD. A third had eating disorders and clinically significant body shape or weight concerns. Thirty percent of those with BDD and shape and weight concerns demonstrated higher levels of depression, anxiety, and suicidality than patients without such concerns. Further, those with shape or weight concerns measured high in rates of

“These children want to hurt themselves. Many come in after attempting suicide.”

post-traumatic stress disorder, disassociative disorder, and sexual preoccupation—findings that suggest past physical or sexual abuse.

Dyl is conducting research that will follow up on these study results. But already the work has made an impact. “The BDDQ is now used as a part of the standard admissions packet at Bradley,” Dyl says. “We’ve found you need to ask these questions. Otherwise these kids won’t talk about it.” — J.A.



### WHO KNEW?

#### Escape from New York

WELL-HEELED LADIES WHO LUNCH and PR-savvy celebrities alike are missing Rob Haskell MD'10 in Manhattan these days. A *New York Times* article once said that approval from the 32-year-old writer could “cement a socialite’s reputation.” As former senior features editor at W, the high-fashion glossy that creates the closest encounters most readers will ever have with stars of film, fashion, and high society, Haskell has traveled in the rarefied circles populated by marquee names like Cameron Diaz, Lindsay Lohan, and Catherine Zeta-Jones. He describes French film legend Catherine Deneuve as “a charmer.” Uma Thurman is “difficult.” Renee Zellweger, he says, is “exceedingly clever”—and not just because she had the good sense to send milk and cookies to St. Vincent’s Hospital when he was volunteering there.

Today, Haskell spends most of his time in Providence, and his interviews, though glamour-lite, are no less gripping. The first-year student is busy training to take histories from patients. “It’s rare in magazine writing that you have the opportunity to write about your subject with perfect sensitivity,” he says. “The moral imperative in a medical interview is so different.”

Haskell began his career in journalism at *House and Garden* before moving on to chronicle the comings and goings of New York’s Social Register for *Women’s Wear Daily*. After six years at W, he embarked on a freelance career, penning articles for *Vogue*, *GQ*, *New York Magazine*, and others. But in 2003 the Yale grad decided he needed

HASKELL, HEE JIN KANG; JESSICA DEANE ROSNER



a new crowd. “The world of fashion and society is just a bubble,” he explains. “You start to feel ... slight.”

Haskell found weightier things in an evening physics class at Columbia University, along with a growing interest in science. “Physics opened that door,” he says. “I felt I was finally confronting the other half of life.” Haskell finished his premedical coursework through Columbia’s post-baccalaureate program, and was accepted to Brown Medical School in 2006. He continues to freelance; at press time he was fine-tuning a feature for *Harper’s Bazaar*.

“It’s a weird thing,” Haskell says of shifting gears from anatomy lectures to pop culture commentary. “I exit the thorax and enter into this different mindset. Someday I’d love to be writing about medicine, too.” — J.A.

PUNCHLINE

Teen Sex and Condoms



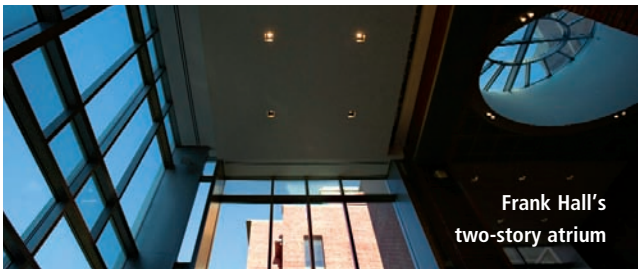
RESEARCHERS AT THE BRADLEY HASBRO CHILDREN’S RESEARCH CENTER and Brown have found that teen attitudes toward condom use with a “main” vs. a “casual” sexual partner are crucial in developing effective HIV intervention programs. The study, published in the *Journal of Adolescent Health*, involved more than 1,300 sexually active subjects between 15 and 21. The number of unprotected sex acts in the past 90 days was substantial and equivalent between the two groups.

The authors state that HIV intervention programs that do not target adolescents’ attitudes and practices related to casual vs. main partners may miss an opportunity to change behaviors. “Unfortunately ... teens may overestimate the safety of using condoms ... with a casual partner and underestimate the risk of unprotected sex with a serious partner,” says lead author Celia Lescano, assistant professor (research) of psychiatry and human behavior.

SPEC SHEET

Science for Life

Floor 5: Neuroscience
Floor 4: Neuroscience
Floor 3: Molecular Biology, Cellular Biology and Biochemistry/Neuroscience
Floor 2: Molecular Biology, Cellular Biology and Biochemistry
Floor 1: Molecular Biology, Cellular Biology and Biochemistry



Frank Hall’s two-story atrium

2-Story Bridge	Floor 3: Postdoctoral and Graduate Programs
	Floor 2: Public Space and Seminar Rooms
	Floor 1: CORE Research Facilities

WHAT DID IT TAKE TO BUILD SIDNEY E. FRANK HALL FOR LIFE SCIENCES? Three years and equal amounts of tenacity and vision—not to mention the ingredients below. At the October 6 dedication ceremony, MIT President Susan Hockfield delivered the keynote address and received an honorary degree.

**SURFACE AREA:** 169,000 square feet (Brown’s third-largest building)  
**CONCRETE:** 64,000 cubic yards (equal to 200 miles of city sidewalk)  
**EXTERIOR WALLS:** 391,000 bricks, 51,000 concrete blocks, and more than four miles of exterior joint sealant

**GLASS:** 35,000 square feet (equivalent to 7.5 basketball courts)  
**HOURS LOST TO INJURY:** 0  
**INTERIOR PARTITIONS:** 240,000 square feet (equivalent to five football fields)  
**STRUCTURAL STEEL:** 3.8 million pounds (the equivalent of

approximately 1,266,666 adult human brains)  
**PUNCHED WINDOWS:** 140  
**WORKER HOURS:** 621,000  
**PARKING TICKETS** received by workers: 0  
**BABIES BORN** to the construction team during the project period: 8

Visit <http://www.brown.edu/Administration/PAUR/media/> for more information. □

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## Back to Basics

# Implicating Insulin

AS POPULATIONS OF DEVELOPED COUNTRIES LIVE LONGER AND longer lives, a perfect storm is brewing that could wreak havoc on public health. While advances in health care have improved life expectancy, diseases of old age will soon affect increasing numbers of people. In fact, by the year 2050, it's projected that 15 million people will be affected by Alzheimer's disease. The indirect and direct costs of Alzheimer's, which are already calculated at approximately \$100 billion per year in the United States, will climb proportionately.

One of the hottest breakthroughs in understanding the etiology of Alzheimer's points to a new culprit causing the devastating effects on the brain, as well as to a new and highly promising therapy: insulin. And some of the leading research is coming out of a lab at Brown Medical School and Rhode Island Hospital.

### TYPE 3 DIABETES

DR. SUZANNE DE LA MONTE, PROFESSOR of pathology and laboratory medicine (research), is a neuropathologist at the Liver Research Center and the Department of Clinical Neuroscience. For years she has studied the effect of alcohol on neurodegeneration, the gradual death of neurons in the brain. She began looking at the role of insulin in the brain in relation to alcohol, an area that had not been well studied. At the same time, she began studying neurodegeneration that specifically leads to Alzheimer's disease.

"We started realizing there were

similarities in what was happening in both," de la Monte says. "That was the first clue that there was something wrong with the insulin actions in the brain in Alzheimer's disease."

In a paper published in the *Journal of Alzheimer's Disease* in early 2005, de la Monte and co-authors provided the first evidence that insulin and its related proteins are produced in the brain and that reduced levels of both are linked to the late stages of Alzheimer's. They concluded that Alzheimer's is actually

"The insulin deficiency isn't coming from the pancreas, it's coming from the brain."

a complex neuroendocrine disease that originates in the central nervous system, and they coined a new term: type 3 diabetes.

"We called it type 3," explains de la Monte, who moved her laboratory to Brown six years ago from Harvard/Massachusetts General Hospital, "because we knew it involved an abnormal response to insulin, but the most important thing to realize is the insulin deficiency isn't coming from the pancreas, it's coming from the brain."

Proving that insulin was, in fact, made in the brain was the first step.

"The brain makes insulin in regions that happen to be sensitive to the neurodegeneration that occurs in Alzheimer's disease. That was the first indication that the deficiency is coming from the brain and not the body," she says.

### ALL ROADS LEAD TO INSULIN

LATE IN 2005, DE LA MONTE AND colleagues published more astounding results, in the same journal: insulin and its receptors drop significantly in the brain even in the early stages of Alzheimer's, and levels decline progressively as the disease becomes more severe.

One of the most exciting aspects of these findings, de la Monte says, is that "when you block insulin signaling it

can explain all of the effects that you see in Alzheimer's disease." As insulin signaling breaks down, it leads to increased oxidative stress, impaired





Suzanne de la Monte

metabolism, and cell death—all causing neurodegeneration.

She and her colleagues found another abnormality, parallel to the decline in insulin levels, as the disease progresses. Insulin and its related protein, insulin-like growth factor (IGF), lose their ability to bind to corresponding cell receptors, creating a resistance to the growth factors and thus causing cells to malfunction and eventually die. Their work shows that insulin impairment is linked to major neurotransmitters (i.e. acetylcholine) responsible for cognition, to poor energy metabolism, and to abnormalities that contribute to the tangles characteristic of advanced Alzheimer's disease.

#### TURNING BACK THE CLOCK

DE LA MONTE SAYS SO FAR THEIR work indicates that you can reverse or prevent the effects of Alzheimer's disease by protecting the cells that rely on insulin and IGF. In a paper published in September, again in the *Journal of Alzheimer's Disease*, she and colleagues showed that peroxisome-proliferator activated receptor (PPAR) agonists prevent several components of neurodegeneration and preserve learning and memory in rats with induced Alzheimer's disease. They found that an agonist for PPAR delta, a receptor that is abundant in the brain, had the most overall benefit.

While they were not able to stop

the deterioration of insulin and its receptors, the researchers were able to bypass the defects in insulin signaling and preserve the cells that need insulin to thrive by administering PPAR. The major effects of the PPAR

treatments for early Alzheimer's, de la Monte would also like to see new assays developed that can detect the early signs of brain insulin deficiency, something as simple as a blood test that can be done in a doctor's office as part of routine health screening. That would insure patients can get these therapies early on in the disease process, when they have the best chance of working.

Research on insulin's role in neurodegeneration has exploded in recent years, largely because of the possibility

**"[I]n the early phases of Alzheimer's, there's a good possibility [patients] could get treatment that will help them."**

treatments were to increase brain size, preserve insulin and IGF-II receptor bearing neurons, and preserve learning and memory.

"If the diagnosis is suspected or patients are in the early phases of Alzheimer's, there's a good possibility they could get treatment that will help them. It's possible that in the moderate phase, treatment will also help, but more work needs to be done to show that," de la Monte says. It's unlikely the treatment will work in the late stages, because the cells have already died.

Of the three types of PPAR agonists used in the study, one, called PPAR gamma, is already FDA approved as a treatment for type 2 diabetes. The two other classes of PPAR agonists have not yet been approved for clinical use.

In addition to developing more

of revealing new drug targets. But not all scientists agree with de la Monte about the mechanisms in play. Some believe the pathway may involve mitochondria, the cell's internal energy factories. Others hypothesize that the insulin deficiency delays the cell's ability to clear away refuse, resulting in the build up of amyloid. There is agreement, however, that boosting insulin in the brain can mitigate the symptoms of Alzheimer's, and that there is promise in this form of treatment.

"If we all get on the same page, even if we differ on the cause, it's OK because the patient is still going to be treated," de la Monte says. "This might be one of the few situations where we don't agree on the concepts but still agree on the final approach, and that's fine."

**—KRIS CAMBRA**



# Dispatches

BY MONIQUE A. ANAWIS '85 MD'90

## MONGOLIA:

### Land of Blue Skies and Unexpected Stories

LAST YEAR, I WENT TO A SMALL BOOKSTORE OUTSIDE CHICAGO TO attend a lecture by Dr. Natsagdorj, a high lama, or Buddhist monk, who is also an honored physician in Mongolia. After his lecture I approached him to ask questions, and we became friends. As a practitioner of ancient Mongolian traditional medicine, he knew of special healings for the eyes and wanted to teach them to me. I should come to Mongolia, he said, and study with him. We continued to share our experiences as physicians until the bookstore lights were dimmed in a subtle sign that it was time to leave.

My private solo practice in ophthalmology, a health law consulting firm I recently formed, teaching, and life in general left me little time for pondering a trip to Mongolia. Lama and I regularly e-mailed each other—a rather surreal experience in itself. After six months, we met again in Chicago and made plans for my visit. I suggested that while being his student, I hoped to share some of my knowledge of

western medicine. I could give lectures and examine patients.

On the long solo journey to Mongolia, I befriended an engineer from Shanghai who carried my bags and guided me through Beijing Airport, where my heavy bag of ophthalmic equipment was completely dismantled. After clearing Chinese customs, the attendant tried to block me from taking my extra carry-on bag

on the next leg of the journey. Again, an intrepid fellow traveler leapt to my aid, shouting, “She’s a doctor on a medical mission! She has to take these supplies on board!” I was certain that his well-intended efforts would land us both in prison. Instead, the beleaguered attendant hurled my 30-pound case at my new friend and shouted at us, “Go! Go!”

That is how, after 21 hours of travel, I arrived at 12:30 a.m. at the airport in Ulaanbaatar (UB), the capital of Mongolia. Looking down a long, steep flight of stairs I saw the gold, orange and blue-trimmed robe of Lama, who greeted me with the traditional staccato inhalation while touching one cheek then the other. Given his social and religious stature and the late hour, I had expected one of his assistants. He just laughed and said, “I told you I would pick you up.”

Wanting to absorb my new surroundings while fighting fatigue, I strained to see the dimly lit roads. Later, I would recall that I never felt the need to adjust; there was a familiarity to this place where I had never been.

My next morning began as most weekdays did. I went downstairs to the cozy dining area of the family-run hotel. Having learned to say “hello,” “thank you,” and little else, my mime skills improved. Some days, the co-owner joined me and we wove together fragments of conversation in French. Then I would be driven to the Manba Datsan (MD), a combination Buddhist monastery, medical school, and clinic with an on-site pharmaceutical factory. The gravel road to the MD was lined with the day’s patients and pilgrims: families, young couples, elderly grandparents with their grandchildren in their best clothes, each of whom came with different wishes. Some asked the lamas for prayers for a loved one or for a successful marriage or business. Some ascended the steps to see the doctors or meet with Lama. He had an endless stream of visitors from all over the





Anawis and Dr. Natsagdorj (center)  
with some of his followers

world; the most memorable was a professor from Warsaw who stared at me in disbelief as I spoke to him in fluent Polish.

My days were filled with teachings, both given and received. I lectured with PowerPoint slides to Lama's medical students and fellow lamas. Even after three hours in sweltering heat, the students had an eagerness and attentiveness that made me marvel. During the short breaks, students gathered around me with questions and later clamored to help carry my equipment.

I also examined patients in tandem with Lama. While he took pulses and asked select probing questions, I used my portable ophthalmic suite and translator's help to unravel patient problems. With two doctors, a translator, and often other family members joining us, we all worked to help the patient. No HIPAA issues here. Our eastern and western approaches were complementary, and

included my bringing two glaucoma patients to Hospital #3, a Western-type medical facility.

I was excited to meet the doctors at Hospital #3, with which Health for Humanity (a charity for which I head the blindness prevention task force) has an ongoing project to develop cataract and other surgical skills. We are their partners in the WHO's Vision 2020 program, which aims to eradicate preventable blindness by the year 2020. While the construction site out front, the stern-faced bust of the Russian physician-founder of the hospital, and its utilitarian name bespoke another era, there was a high level of professionalism and patient care at this hospital. The nurses were all meticulously attired in the same light green uniforms and white caps. Patients were three or four to a room, sometimes with men and women in the same room. All of the doctors and

nurses were women, in keeping with the Russian system.

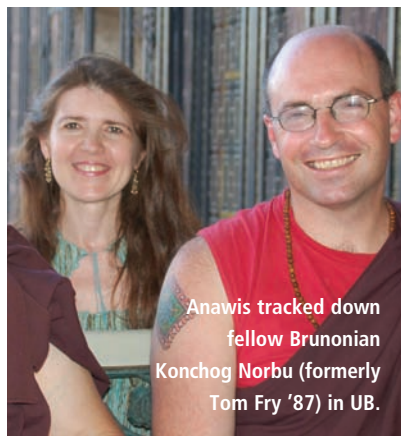
My colleagues, like my students, were eager to have me examine patients and review their care. In the eye clinic, ocular trauma is by far the most common problem. Given the nomadic existence of many Mongolians, it usually takes several days to reach the city hospital, often resulting in disappointing outcomes despite conscientious medical care. Resources are limited in this tertiary care center, with one CT scanner, no MRI, and antibiotics restricted to penicillin, ampicillin or chloramphenicol. The clinic has one slit lamp, one illuminated eye chart, one ultrasound, one tonopen (usually unused given the scarcity of batteries), and an assortment of hand-held, antiquated pieces of equipment. The only ophthalmic laser in the country is used in a private practice. I was pleased to bring a new



## Dispatches

pachymeter (a device for measuring corneal thickness) thanks to a donation from DGH Technology, Inc. We are working to equip both the clinics and the operating rooms.

What is Mongolia like? UB reflects the transitions of its people. Beside ancient pagoda-style temples sit dreary cement Soviet-era buildings and futuristic glass structures. The people have a respect for cultural traditions and religion, recall their years of Soviet occupation with mixed emotions, and

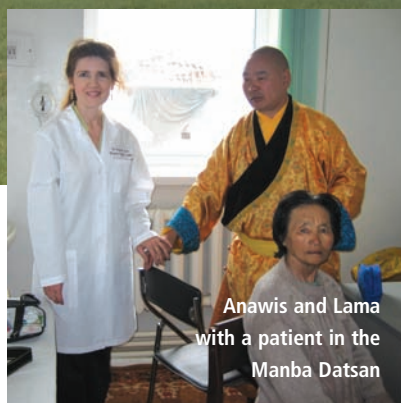


Anawis tracked down fellow Brunonian Konchog Norbu (formerly Tom Fry '87) in UB.

My days were filled with teachings, both given and received.



A Mongolian herdsman in the countryside



Anawis and Lama with a patient in the Manba Datsan

are working to bring prosperity and modern ideas to their society. In UB, I met with Konchog Norbu (Brown '87), whose calling as a Buddhist monk had led him there. Somehow meeting a fellow Brunonian halfway around the world seemed fitting.

In sharp contrast to the dust kicked up by construction and the traffic of UB, the countryside reclines in solitude. As paved roads recede, the mountains, rutted terrain, and captivating quiet take over. Lama and I drove for hours without seeing buildings or other people—just timeless scenes of wandering horses, camels, yaks, and sheep cooling off in the rare

pond. We listened to music, stopped for photos, met Lama's followers and prayed atop a mountain. We met colleagues and saw their patients who were cared for in small out-post hospitals or in gers equipped as treatment centers. On one very special occasion, we stopped so that Lama could sing a song honoring my mother, which we taped as a gift for her.

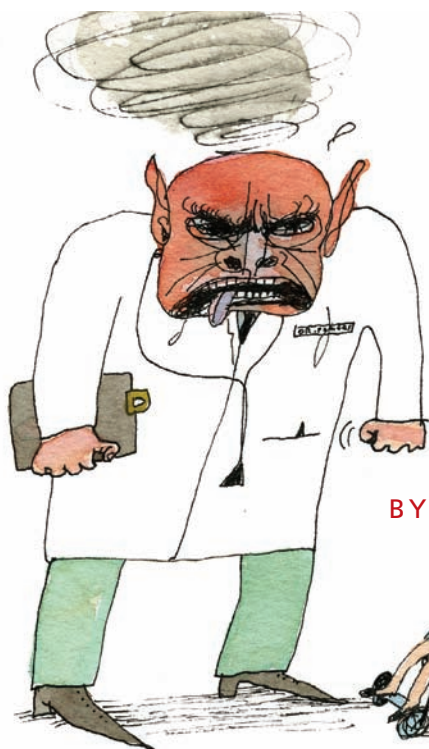
My trip was a series of human connections: new friends met through the generosity of Lama and the privilege of our profession. Among the extraordinary people I met were a grateful mother and child in the countryside whose experiences would help me bring another child to the U.S. for medical treatment. Oyunjargal, only 2 years old, had open-heart surgery sponsored by the Rotary Clubs of New Jersey and UB. Months later, I received an urgent e-mail from Punsaa, my friend and translator in Mongolia, asking for help for her friend's 12-year-old child with leukemia. I phoned Oyunjargal's sponsors and countless others seeking help. Through the kindness of colleagues, friends, and Rotarians, we navigated the complicated political system against incredible odds.

Nyamtasuren—a new name, meaning “long life,” given to Oyunjargal by Lama's assistant lama—is now in my home city of Chicago receiving a two-year course of chemotherapy. Her journey and mine are inextricably woven together. Her doctors, family, interpreters, and I have a long road ahead of treatments and fundraising to provide for her care. Even as we help her and her family get used to Chicago and to U.S. medical care, we honor their Buddhist traditions and beliefs. My skills at miming have since been supplemented by more Mongolian words. Through cell phones and e-mails, we are in touch with her relatives and my friends in UB.

Lama has asked me to be his consultant in planning an eye clinic in Mongolia combining traditional Mongolian medicine with western ophthalmology. My future is not as I would ever have imagined it as I drove to a small suburban bookstore more than a year ago. □

**Monique A. Anawis '85 MD'90, JD,** established a charitable trust for Nyamtasuren and other overseas patients in need. E-mail her at [moniqueanawis@earthlink.net](mailto:moniqueanawis@earthlink.net) for more information.





# The Angry Doctor

BY TOM DOYLE MD'03 HS'06

A WHILE AGO I FINISHED A MONTH-LONG ROTATION IN A LOCAL emergency department. A common ER scenario is the point when a patient needs to be admitted to the hospital for diagnosis X, but it is unclear to which service—surgical, medical, renal, etc.—the patient “should” go. Admitting physicians can be skeptical of stories they hear from the ER—patients admitted from the ER are often not physically seen in the department by a doctor from the admitting service, and ER volume and acuity can be such that patients are inappropriately admitted or sent to the wrong service, or diagnoses are missed altogether. Of course, many of these situations also arise elsewhere in the hospital.

However, the stakes are high, especially in the ER. Patients are acutely sick, families are stressed, diagnoses are often unclear, and interactions can be tempered by guardedness of care providers meeting each other for the first time.

During one of my ER shifts last year, I made a total of 11 calls to providers involved in the care of a single dialysis patient with a cardiac history who came to the emergency department after sustaining a hip fracture during a fall, the cause of which was unclear. In the three hours that elapsed as I attempted to admit the patient—describing the patient's presentation and work-up multiple times—I felt I became the locus of vitriol on the part of these physicians whose ostensible goal was to care for a

patient in a hospital where each of them had admitting privileges.

Even now, more than a year later, I can hear a virtual cacophony of the doctors I talked to that day—repeating, edgily, in turn, like a mantra, “Is this patient really *appropriate* for my service?” Each then requested that I contact another of the physicians involved in the patient's care and ask that physician to admit the patient. Not one of the physicians I spoke with from the emergency department said, upon hearing the case, “Yes, I will admit and take responsibility for this patient on my service.” One physician finally “agreed” to admit the patient, hanging up the phone in a fit of pique: “They always do this! I can't believe it!”

## Resident Expert

I imagined my patient, lying semi-comfortably on the stretcher after a liberal amount of morphine, listening to our discussions.

“Are they angry at *me*? Why doesn't anyone want me on their service?” he might legitimately have wondered.

No one likes an angry doctor. Anger must rank a close second only to incompetence among attributes patients dread in their physician. The specifics of the admission of this particularly complicated patient aside, the experience left me with a sense of frustration and made me wonder what unintended consequences might follow in the wake of the displaced anger displayed by the feuding admitting doctors involved in caring for this patient.

The root causes of physician frustration are multiple—medical knowledge grows exponentially while individual practice areas become increasingly sub-specialized; years of requisite training accrue educational debt and the psychological debt of loss of time away from family and personal interests; physician reimbursement for medical care can be dramatically lower than that of professions that require a fraction of medicine's time and emotional commitment; and, finally, many argue that the overall prestige of the medical profession has eroded.

What can be done? I don't have answers other than what I tell myself when I have a troubling interaction with a colleague or an especially stressful day: to remember that the subtle and corrosive effect of anger is to diminish communication, whether it is in an OR, on ICU rounds, in requesting a consultant's input, or during admitting triage in the ER. I also remind myself that succumbing to anger will in the end only result in diminished patient care. □

**Tom Doyle** recently completed training in the general internal medicine residency at Rhode Island Hospital/Brown Medical School. He is currently an internist at the New Bedford Community Health Center in New Bedford, MA.



## Close Up

# A Purpose-Driven Life

BY KRIS CAMBRA • PHOTOGRAPH BY KAREN PHILIPPI

IF YOU WERE FACING A CANCER DIAGNOSIS, WOULD YOU RATHER have the kindest doctor in town or the smartest?

What if you didn't have to choose?

The Program in Women's Oncology at Women & Infants Hospital and Brown has a hard-won reputation for providing the highest standards of cancer care. But they didn't get there by worrying only about p-values and the five-year survival rate. Chemo and radiation, surgery and consults, as they say in their guiding philosophy, are the form of their work but not the essence. That there is a balance between caring and curing, that you can at once provide the highest level of technical expertise and the highest level of tenderness and concern—these are the hallmarks of this program.

And behind it all is an unassuming Vermonter with a curious name: Cornelius O. "Skip" Granai III.

### A HANDSHAKE AND A PRAYER

BY 1990, SKIP GRANAI WAS WHAT YOU might call "successful" in the world of academic medicine. After training at Tufts, he was on staff at Mass General with a faculty appointment at Harvard. It was the dream job he thought he would never leave.

Then he got a call from former Women & Infants' CEO Tom Parris. The hospital wanted to start a program

in gynecologic oncology and Granai had come up on the radar as a possible founding director. But Granai wasn't interested. After a couple of persuasive phone calls, he agreed to come down to Providence to talk with Parris about heading up the program. But he warned the tenacious CEO that there was no way he'd take the job.

Instead of the whirlwind tour of hospital and campus most academic job interviews entail, Granai found himself meeting one-on-one with Parris in his office outside the hospital. Their conversation lasted three hours.

"I hadn't seen the university or the hospital, hadn't even met a doctor, but now I was interested in an idea. I listened to what he was thinking about and the values he was expressing, and the potential of those values, and I was inspired," Granai says.

By the time he drove back to Boston, Granai was praying that he'd get a call back. And when the call came, he packed up his family and left all the things he said he'd never leave, "basically, on a handshake."

With three colleagues from Mass General, Granai set up an oncology practice at Women & Infants'. After spending its first century devoted to obstetrics and improving maternal and

neonatal health, the hospital for the first time would turn its attention to the other end of the lifespan, and provide care to women with cancer. The culture clash was immediate, and unanticipated.

The staff, once consumed with the relatively "happy" events of obstetrics where they rarely saw adult patients dying, was now faced with 65-year-old women dying of ovarian cancer. "Nurses were saying 'This isn't the job I signed up for.' They felt we were changing the complexion of the hospital," Granai says. Oncology's place at Women & Infants' was openly challenged. And it was the same CEO who was responsible for bringing it there who stood beside Granai and reaffirmed the hospital's commitment to providing cancer care.

"I learned from that experience how important teams of people are. You can have a wonderful idea and all the values in the world, but you still need to bring them to life, and that takes all kinds of people to come together," Granai says.

### P-VALUES

WITH THE ADMINISTRATION BEHIND him, Granai could turn his efforts toward creating a world-class program in gynecologic oncology.

Handsome and prematurely white-haired, Granai is a soft-spoken philosopher. Nothing, it seems, is left unconsidered, nothing taken for granted. What the Program in Women's Oncology has become is the result of Granai's constant reevaluation, deep reflection, and logic, all based on a mandate for creative thinking and open-mindedness. He's distilled his





"We are honored by those who want us and allow us near  
at their most intimate moments." —SKIP GRANAI



## Close Up

beliefs into some simple questions, and asks his physicians and staff to revisit these again and again: *What would we want done for our loved one under these circumstances? Can we do more?* The answers to these questions form the values of this program.

Undoubtedly, top-notch treatment would be the first thing anyone would want for a loved one, treatment that has the greatest chance for cure or prolonging life. These are the p-values—the evidence-based medicine that has been shown to be most effective in treating women's cancers. The Program in Women's Oncology is one of the largest clinical programs in New England, drawing patients from Cape Cod to Connecticut.

"We have a team of people who are committed to the best of the science of medicine," Granai says. "You have to have that. It's incredibly central to giving people the best possible care."

The Program supports research studies from basic science to translational, where experiments that have worked in the laboratory are applied to patients, and clinical trials. The Program is part of several national clinical trials groups, offering its patients the opportunity to take part in the most current experimental treatments. Researchers also pursue novel studies

top residency programs. Granai says that while fellows are there to be trained in the technical aspects of surgery and patient care, what they are really doing "is becoming health care leaders." They become informed about such issues as health care rationing and are taught to put their passion for their patients to use as advocates for better health care. The Program also boasts one of the few fellowships in breast cancer, a testament to the Program's "whole patient" approach to women's health.

"We know we are offering a high standard of care today. But what are we going to do tomorrow?" he asks.

### CAN WE DO MORE?

FOR GRANAI, THE ANSWER IS ALWAYS yes. Even when all of the medical options have been exhausted, when a patient's physical needs have all been met, there is still more that can be done. That's where the "h-values"—human values—come in.

The Program in Women's Oncology offers more than just the standard approaches to cancer care. The program is entirely patient centered, and focused on what patients need at every step of their diagnosis and treatment, beyond the given of the best in technical care.

treatment process. All of the social workers have special training in oncology. The department offers numerous support groups and an Extended Counseling Service for those in need of extensive one-on-one therapy.

Patient advocates assist with the harsh impact cancer can have on real life issues, such as job loss, insurance difficulties, transportation needs, and financial aspects, among other things. "Our patient advocates are routinely on the phone with the electric company, the gas company, contesting shut off notices," Thompson says.

And then there's the complementary care. On any given day, therapy dogs can be found sitting in the laps of people receiving chemotherapy infusions. A massage therapist is on site to offer massage and lymphedema therapy (lymphedema occurs when lymphatic fluid pools in the arms or legs after cancer surgery or radiation to the lymph nodes). There's Reiki, yoga, an expressive arts group, and soon, music therapy.

Granai says that while there is evidence of many of these practices providing a benefit, including some research they conducted themselves on the impact of massage, the clinicians never make unrealistic promises. "Massage isn't going to cure cancer," he explains. "But even if it doesn't change the outcome, it changes the moment."

These services are not some ancillary option available to those patients who seek them out. They are the Integrative Care Program, and part of the standard course of treatment for those who wish to partake in them.

"The first thing that Skip said to me when I came to work for him was, 'I want you to make this program the model for oncology social work across the country,'" recalls Thompson. Intimidated at first, she was soon inspired by the challenge.

That's not to say he's always the easiest person to work for, Thompson says, admitting that they sometimes butt heads. "It's hard when someone has a clear vision and is so passionate.

**"Massage isn't going to cure cancer.  
But even if it doesn't change the outcome,  
it changes the moment."**

on new molecular compounds that might be effective in killing cancer cells, and genetic analysis of cancer.

In addition to teaching Brown medical students and residents, the Program offers a four-year fellowship in gynecologic oncology that enrolls one fellow per year, usually from a candidate pool of 100 applicants from

Diane Thompson, MSW, LICSW, directs the program's social work department, leading four clinical social workers and two patient advocates. A social worker meets with every patient before her diagnosis, is present at the family meeting where treatment options are discussed, and continues to accompany patients throughout the



Like when he told me to come up with a business plan for the social work department, and I told him I'd never done anything like that before. 'Figure it out,' he said."

And she did. Thompson says that Granai allows the conflict and the angst to exist "to bring out the genius in everyone. His success is a testimony to that philosophy."

He knows something of allowing creativity to flourish, to step out of the way of capable people with good ideas. That's what Tom Parris did for him.

#### PHYSICIAN AND FRIEND

AFTER THE INITIAL DIFFICULTIES, Granai soon found himself surrounded by a dedicated nursing and professional staff who shared his values for service to patients. He—and they—unashamedly invoke the word "family" when they describe their work environment and their relationships with patients.

Granai struggles to find words that adequately describe his staff's commitment. "The people that work here wear their hearts on their sleeves. They'll go down to brush the snow off somebody's windshield. It doesn't take much to show that there's caring here beyond the average," he says.

The respect is mutual. "It's a privilege for me to be with him when he is talking to his patients," says Thompson.

She recalls one young woman who was diagnosed with cervical cancer and had no family in the area. Throughout her treatment, the patient had never asked about dying. One day, near the end of her life, she was meeting with Granai and Thompson about what the next steps were.

"I remember she couldn't get the words out. She was whispering, and Skip had to put his face close to hers to hear," Thompson says. "And she finally got it out, but she was practically just mouthing the words: 'Am I going to die?'"

Without hesitation, Granai leaned in closer and whispered back to her "profound, reassuring truth."

What seems like an uncanny knack for anticipating his patient's needs—when they need hard facts, when they need a hug—is, in truth, part of knowing a patient as an individual, taking time to see not only her cancer, but who she is as a woman. It's part of the poem, written by Granai, that has become the mission statement of the program: "We are honored by those who want us and allow us near at their most intimate moments." And those include their dying moments.

"We're always going to funerals and we're always mourning. I don't understand a cancer program that doesn't

Granai says his ideas are not original or uniquely held, that given a moment for introspection, these values resonate with anyone who truly cares for others.

#### HOW DO WE KNOW?

"NONE OF US COME FROM NOWHERE without any help," Granai says. Family has both shaped and grounded him. His father was a small town family doctor who imparted "old Vermont values." Today, he finds solace and what he calls "true friends" in his wife, Cheryl, and their four grown children.

Poetry, too, has helped Granai work through the intense and profound

**"We go to serve in spite of our own fears  
because we believe in the goodness of it."**

mourn," Granai says. "There's this sense that you have to be professional, and yeah, you do, but the fact is, if you're not bothered by what you see you're missing the point. It can't be that it's not sad."

What makes it easier, he explains, is the knowledge that what they do for patients is intrinsically good. "You watch those nurses, they are at the bedside of dying patients all the time, they have their own fears, of course they do, but they show up anyway. None of us are actually up to that, but in our own hearts as doctors, I think we should be afraid. You're just a person.

"We go to serve in spite of our own fears because we believe in the goodness of it."

Granai believes that the values he espouses are universal, though they may remain just below the surface. He's invited to speak around the country, and audiences with a wide variety of experience, from eminent scientists to unflappable U.S. Army surgeons, have embraced his talks, sometimes with tears in their eyes, remembering their own patients or loved ones.

emotional conflicts of his work. He recalls being upbraided by a dying elderly patient when he, trying to reassure her as she suffered the indignities of end-stage ovarian cancer, told her "I know how you feel."

He realized immediately that that was not what he meant. He wasn't a woman, suffering with disease, about to leave people she loved. But he knew enough about himself to know how he would feel in her situation.

"I am afraid of cancer. I am afraid of my own death. Those are things I'm not proud of but things I've come to realize and have tried to integrate into my thinking," he says. He wrote her an apology:

*Right now you're afraid.*

*How do we know?*

*Because we would be, too, be afraid.*

*There is time, and in it you will see Elegantly simple wisdom will return*

*And you will again proceed with grace.*

*Right now, though, you can rest here among friends.* □



# You and Me and Everyone We Know

How Diabetes Is Defining Generations

BY KRIS CAMBRA

MODERN MEDICINE LICKED POLIO, CURTAILED HIV, and even made gains on cancer, but all of those advances in public health are being threatened by a non-communicable chronic disease: diabetes.

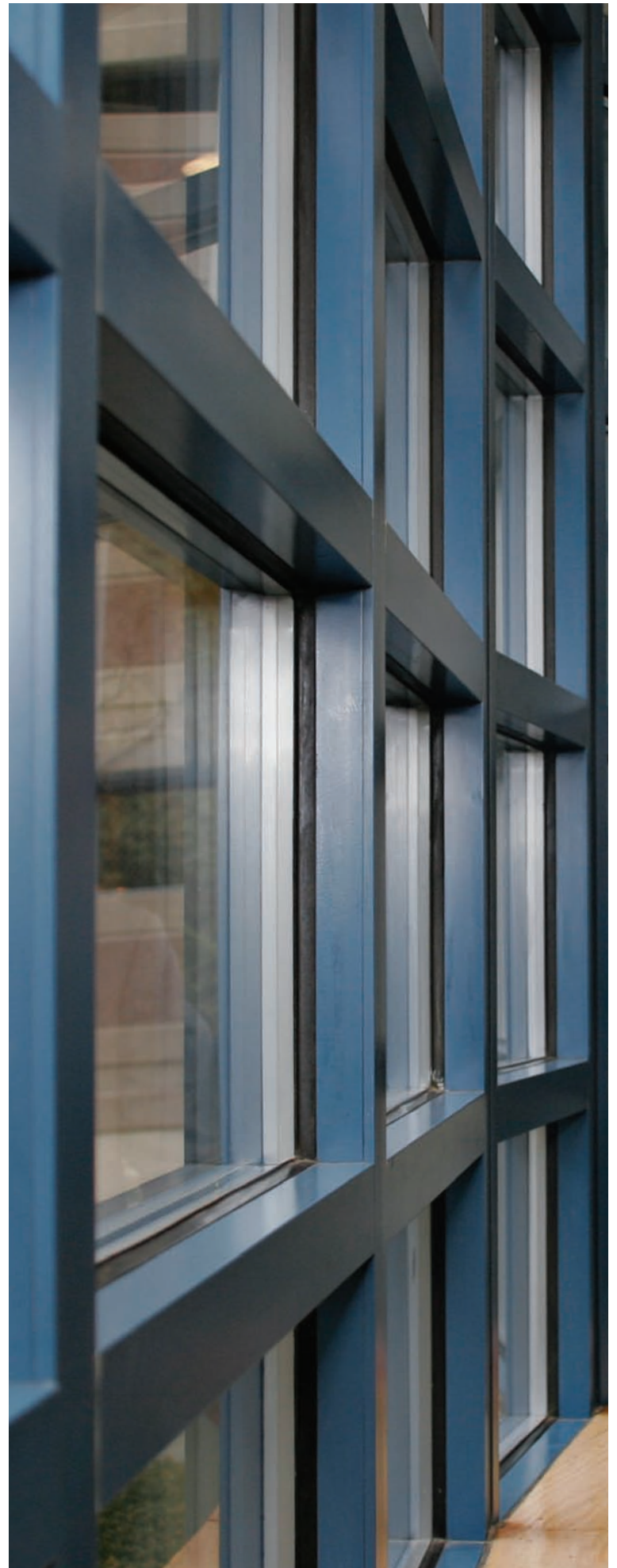
The numbers are shocking: in the United States, 1.5 million new cases of diabetes in people 20 years or older were diagnosed in 2005. Over the past several decades, the prevalence of diabetes has increased an astounding eight- to ten-fold. It occurs most often in older people but, of great concern, the percent increase in new cases each year is now highest in children and young adults. The numbers parallel another disturbing health trend: the steady increase in the number of Americans who are overweight or obese. Today, that's two-thirds of us.

In the past six years, top experts have been recruited to Brown Medical School to establish a center of excellence for the treatment and study of diabetes. Combining clinical care, basic and clinical research, and medical education, faculty members offer comprehensive services to the people of Rhode Island while advancing knowledge in the field and training future physicians and researchers.

## Leading the Way

PROFESSOR OF MEDICINE ROBERT J. SMITH, CHIEF OF THE Division of Endocrinology and founding director of the Hallett Center for Diabetes and Endocrinology at Rhode Island Hospital,

PHOTOGRAPHS BY LUCAS FOGLIA







Robert Smith at  
the Hallett Center  
for Diabetes and  
Endocrinology



keeps an eye on the epidemic from his offices in the Coro Building in Providence's Jewelry District. A researcher and clinician, Smith came to Brown in 2000 from the renowned Joslin Diabetes Center in Boston and Harvard Medical School to start the clinical, teaching, and research enterprise here.

The Hallett Center is Rhode Island's only comprehensive diabetes research and treatment program based in an academic medical center. About 7.5 percent of the state's population has diabetes, a rate slightly above the national average, which is estimated at 7.3 percent. This means that more than one in every 14 people in Rhode Island has diabetes. Among people above age 60, one in seven has diabetes, and these numbers increase to one in four for some high risk groups. Rhode Island's higher concentration of elderly residents, lower socioeconomic status, and diverse ethnic composition contribute to the problem.

Of the two major forms of diabetes, type 2 is far more prevalent. Type 1 diabetes is an autoimmune disorder that causes the body to attack its own pancreatic beta cells, destroying the ability to make insulin. Only about 5 to 10 percent of people with diabetes have type 1. In type 2, there is usually a partial loss of insulin, and the body's ability to use it

## Products of Our Environment

THE ENDOCRINE SYSTEM IS ONE OF THE body's most finely tuned orchestrations. Its myriad responsibilities include regulating the hormones that enable us to use glucose—the fuel of life—from the food we eat. Failures at any step can result in deleterious, and even deadly, consequences.

Smith, who works mainly in the area of diabetes but also on related problems that affect human growth, looks at this as a genotype/phenotype problem. He's not

only interested in learning how to help the patients he sees with diabetes, he wants to know why the disease behaves as it does. And that, he says, requires understanding the interplay between two things: genes and environment.

"We believe that both obesity and diabetes result from a combination of strong genetic effects and strong environmental effects. We are beginning to identify the determining genes, but it's difficult because there are multiple ones," he says.

Complicating this genetic predisposi-

tion is what nutritionists call an "obesogenic" environment, one that "gives rise" to obesity. An abundance of high-calorie, high-density foods are available cheaply, while produce and good cuts of meat have a much higher per-portion cost. Quantities, composition, and marketing of food have changed significantly since the 1960s. Meanwhile, cars, the availability of "on-screen" entertainment, and office

jobs encourage sedentariness. Of course, not everyone who lives in this environment becomes obese. Many genes control diabetes and obesity risk, but Smith says those most at risk are those who have genes predisposing them to diabetes.

## Slow Going

DAY TO DAY, SMITH AND HIS COLLEAGUES at the Hallett Center face the hard fact that many of their patients are not successful in losing weight, and for those who are, the loss is often impermanent. For people who are obese—and one in

**"We often do better in managing diabetes than we do the underlying problem of obesity."**

four of them have diabetes—achieving and maintaining weight loss is difficult.

With many recent advances in diabetes drugs, it's often possible for people to achieve excellent control of their blood sugars. But Smith says, with some resignation, "We often do better in managing diabetes than we do the underlying problem of obesity. It's maybe the most frustrating thing I confront in practice—the obesity component. I'm very sympathetic to people with obesity. I see it as a profoundly difficult problem for people to deal with. Obesity is an environmentally induced disease, and not a consequence of some kind of personal failure."

Unfortunately, patients who have not been following their diet and exercise plan will sometimes avoid seeing their doctor. Smith knows "some don't come to see me because they are ashamed. They'll hide from me. Of course that's the worst thing because now they don't have any medical help and their obesity is continuing. That's a scary, difficult problem."

Although dealing with obesity can be frustrating for physicians and patients, he stresses his belief that we will do much better in the near future. The mecha-

**"Of the teenagers diagnosed with new-onset diabetes, about 50 percent are type 2."**

effectively. The recent surge in cases of diabetes has been mainly type 2.

For reasons not entirely understood, diabetes and obesity go hand in hand. Approximately 80 percent of people with diabetes are also overweight or obese, according to Smith. "Clearly, there is a relationship between [them]. We need to address both of those problems at the same time," he says.

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Smith in his lab in the Galletti building.

nisms that control appetite and body weight—much as a thermostat controls temperature—are rapidly being defined and represent new targets for the treatment of obesity. Even modest weight loss, such as 20 or 30 pounds in someone obese, can substantially improve diabetes.

While there are drugs on the market that help people lose weight, none works all that well.

“At present, we can’t administer a magic pill that enables people to effectively lose weight ... And if—or rather, when—there’s success in developing really effective medications we will aggressively pursue that as something we offer people,” Smith says.

A dietician at the Hallett Center coordinates efforts to help patients achieve weight loss, frequently referring them to community programs that focus on behavior modification strategies. Brown’s Weight Control and Diabetes Research Center, directed by Professor of Psychiatry and Human Behavior Rena Wing, represents another valuable resource. Wing and her colleagues develop strategies to help people achieve lasting weight loss that will have a positive impact on their health. Smith says, “Dr. Wing’s pro-



Seeing patients at the Hallett Center.

gram provides both intellectual synergy with us and a place we can refer Hallett patients for participation in weight loss studies.”

## A Ripple Effect

SINCE IT MOVED FROM RHODE ISLAND Hospital to its new location in 2003, the Hallett Center has grown three-fold, and now sees about 11,500 patients a year. It offers a comprehensive program where team members devise the newest treatment strategies and the newest drugs, while delivering clinical care. Its physicians concentrate both on fixing the blood sugars of patients and on managing other factors that influence the complications of diabetes, such as blindness, kidney failure, and vascular disease. In essence, they offer one-stop shopping for people who have not only diabetes but its numerous related issues.

“If a patient comes to the Hallett Center, in addition to seeing one of our six diabetes specialist/endocrinologists, they also can see a kidney specialist, an eye specialist in an adjacent office, a podiatrist, and a member of a team or a whole team that is working on weight reduction. Or they can enroll in a structured patient education course,” Smith says.

That’s critical, because diabetes can lead to a series of life-threatening—and costly—conditions. When last tallied, in 2002, by the American Diabetes Association, annual direct and indirect costs related to diabetes management totaled \$132 billion.

For one, people with diabetes are at very high risk for cardiovascular disease, says Smith. Approximately three of every four people who have diabetes ultimately die of cardiovascular disease. “If you have diabetes, you have the same risk of heart attack as some-

body who has already had one heart attack. It is an equivalent-magnitude risk. It’s huge.”

Other complications include damage to the retina; diabetes is the most common cause of new-onset blindness in adulthood in the U.S. Half of all people on dialysis are there because of diabetes. Diabetic neuropathies attack every part of the body, causing impotence in about 50 percent of men who have longstanding diabetes and contributing to amputations of the extremities.

The cost and level of disability caused by these complications threatens to overwhelm the health care system as people develop diabetes earlier in their lives. An article in the journal *Pediatrics* in 2005 reported that of all the new cases of diabetes diagnosed in children, about 45 percent now are obesity-related type 2. Last year, the pediatric endocrinology service



# America's #1 Export

THE TINY SOUTH PACIFIC ISLANDS OF SAMOA AND ITS COUSIN, AMERICAN Samoa, make for an interesting “natural experiment” to test the impact that modern lifestyles have on levels of obesity and diabetes.

Both Samoas experienced the abrupt infiltration of the modern world during World War II, when Allied troops were billeted to the islands. But American Samoa, a U.S. territory since 1900, became distinctly more modernized, while the sovereign nation of Samoa clung longer to its traditional Polynesian roots after the troops departed.

Dr. Stephen T. McGarvey, MPH, professor of community health, first went to the Samoas as a graduate student 30 years ago to document indications that Polynesians showed pronounced tendencies toward obesity and type 2 diabetes when they came in contact with the ways of life in developed countries. McGarvey began studying the levels of body size, overweight, obesity, and other cardiovascular disease risk factors such as diabetes, elevated blood lipid levels, and smoking.

“People got a taste of this other way of life. Cash came in and they became much more economically developed,”

“We’ve been looking at the temporal trends of the changes in these risk factors and trying to understand what aspects of behavior, the culture, and nutrition and physical activity have had an impact on this,” McGarvey says.

McGarvey has been studying genetic factors that may make Samoans more susceptible to obesity. Could island-bound Polynesians have evolved to become better storers of fat and calories to sustain them through food scarcity and the long, ocean voyages of discovery and settlement?

Either way, the levels of overweight and obesity have reached alarming rates. In American Samoa, in 2002, about 60 percent of men and almost three-quarters of women were obese. Less than 10 percent of American Samoan women were a normal weight

of use to the Samoans as they try to intervene in some of these trends.”

New collaborations with Brown faculty members who have expertise in behavior change intervention studies are making it possible for McGarvey to do just that.

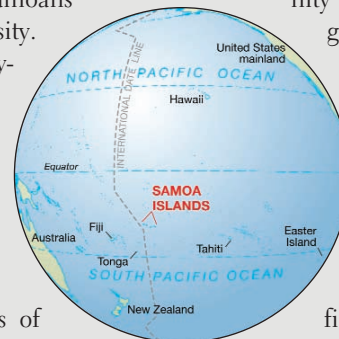
With funds from the National Institutes of Health, McGarvey has teamed up with Drs. Judith DePue, Raymond Niaura, and Michael Goldstein of the Department of Psychiatry and Human Behavior, and Dr. Rochelle Rosen, a cultural anthropologist at Lifespan’s Centers for Behavioral Medicine and Health Promotion, to design a culturally sensitive intervention based on the community health worker model. The

goal is to improve the management of diabetes by training groups of community health workers to be intermediaries between the clinic and the individuals with diabetes and their families.

McGarvey says the first year of the four-year grant will be spent doing “qualitative work to understand what people’s values, attitudes, and knowledge are about diabetes so [the health workers] can give advice and guidance that fits their current knowledge about diabetes and taking care of themselves.” That’s critical in designing a program that informs and educates Samoans in a manner most acceptable to them.

Additional grants are being sought to study adolescent overweight in American Samoa. Much like in the U.S., there has been a distinct rise in childhood and adolescent obesity levels.

While McGarvey holds out hope that they might find something unique about the Samoan genetic susceptibility, the reality is “the genes in Samoa didn’t change as much in the last 50 years as their nutritional environment.”



**“The genes in Samoa didn’t change as much in the last 50 years as their nutritional environment.”**

McGarvey says. “More and different kinds of foods became available, with more processed nutrients and higher fat content, and at a relatively low price.”

With the introduction of wage and salary jobs, people were no longer fishing and farming. Levels of physical activity decreased. Energy expenditure went down and energy intake increased.

for their height. Along with these marked levels of adulthood overweight and obesity, Samoan people suffer from high levels of cardiovascular disease, type 2 diabetes, and other associated metabolic disorders.

After years of doing epidemiological studies, McGarvey says, “[A]t a personal level, I don’t want to just do this etiologic research but do something that will be



began seeing its patients in the Hallett Center's facility. The pediatric program operates under the separate leadership of Dr. Charlotte Boney, associate professor of pediatrics, and follows approximately 500 patients with about 80 new diagnoses per year. Boney says that, "Of the teen-

core components of the Hallett Center's program. Smith says they have participated in promising national clinical trials of new treatments for diabetes. "We're trying to work at the interface between drug discovery and its implementation in humans," he says.

## The American Diabetes Association predicts that diabetes will shorten overall life expectancy in the U.S. for the first time in a hundred years.

agers diagnosed with new-onset diabetes, about 50 percent are type 2."

Seeing patients at Hallett has a distinct advantage, she believes, to facilitate "the seamless transition of care from pediatric to adult practitioner when the adolescent is ready, no matter what kind of diabetes they have."

"The adolescent obese type 2 diabetic is a major new problem," Smith says. "They don't develop diabetes when they're 60 and live with it for 20 years. They get it when they are 15, and if they live a normal lifespan, they'll have it for 65 years. I don't think they are going to be much different than the type 1 diabetic in terms of the potential ravages of the complications, except we're looking at huge numbers."

But it's unlikely these kids will live a normal lifespan, as diabetes is known to prematurely end lives. The American Diabetes Association predicts that diabetes will shorten overall life expectancy in the U.S. for the first time in a hundred years.

### Unlocking the Door

"WE WANT TO UNDERSTAND THE fundamental causes of diabetes and how to treat it, and bring our patients absolutely the best possible and most current medical care. Those are our fundamental goals," Smith says.

That's why research and teaching are

Four investigator-based laboratories look at endocrine disorders at the molecular level, asking basic questions about the underpinnings of diabetes. What makes insulin work? What causes insulin resistance in obesity? One research group, directed by Professor of Medicine (Research) Eduardo Nillni, looks at neuropeptides involved in controlling metabolism and appetite. Assistant Professor of Medicine Haiyan Xu's group is studying how fat tissue drives an inflammatory response in the body, which contributes to certain complications of obesity and diabetes such as cardiovascular disease.

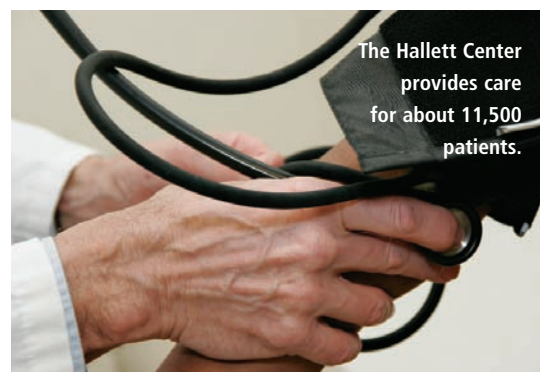
Smith's own lab studies insulin and a related hormone, insulin-related growth factor-I (IGF-I). "We want to understand how these interlinked hormones normally function and what goes wrong when they stop working in human diseases," he says.

Recently, he and colleagues cloned a new protein involved in the insulin and IGF-I signaling pathways. When they looked for links to human disease, they found mutations in this protein in people who have familial Parkinson's disease. There's been a poorly understood observation that people with diabetes develop Parkinson's disease about twice as fre-

quently as people without diabetes. The discovery of these mutations adds more evidence that insulin plays a critical role in the central nervous system, and that disturbing its action can cause neurodegenerative diseases (see Back to Basics, page 10).

The Division of Endocrinology ensures that the lessons learned from research and patient care are put to use training future endocrinologists. The Division offers a clinical fellowship program that has grown rapidly in reputation in the past few years. Two fellows per year are accepted for the two-year program, and applicants are coming in from the top residency programs in the country.

Teaching is also a core component of the program. Smith and his colleagues in the Division of Endocrinology provide classroom teaching for medical students,



and extensive patient-based teaching for residents and medical students.

### The Road Ahead

IT MAY SEEM PHYSICIANS LIKE SMITH are swimming upstream against an unrelenting epidemic, especially when roughly 90,000 people are suffering from diabetes in Rhode Island alone. But he feels advances in medications and basic research provide many reasons to be hopeful. "Of course we would like to have ways to prevent or completely cure diabetes and obesity, and I firmly believe this will come," he says. □



## Essay

BY CHRISTINE MONTROSS MD'06

# The Great Teachers of Anatomical Donation

Medical students in Thailand have a special relationship with their cadavers.

TO THE AMERICAN MEDICAL COMMUNITY, THE first year of medical school conjures immediate images of the rite of passage that is gross anatomy lab. For us, the class centers around cadavers that are metaphorically—and sometimes quite literally—shrouded in anonymity. However, a very different model of human dissection exists in Thailand.

The majority of the Thai people are Buddhist, and due to their belief in reincarnation, there is a cultural reluctance even to donate organs for transplantation. Nonetheless, Thai medical schools benefit from cadavers which are, without exception, voluntarily donated. A 2004 paper from the *British*

*Medical Journal* by Andreas Winkelmann and Fritz H. Güldner explains that the Thai culture deeply respects teachers “to an extent unfamiliar to Westerners,” and every Thai donor is granted the highly esteemed status of *ajarn yai*, meaning *great teacher*. Two ceremonies bestow this status: a dedi-

cation ceremony which occurs prior to dissection, and a cremation ceremony which occurs at the course’s end.

In the dedication ceremony, Buddhist monks and family members of the deceased join students and faculty members in the dissecting room, to chant and pray. The names of the donors are read aloud as the title of *ajarn* is conferred, and each cadaver is given a bouquet of flowers. In a symbolic act of giving to the deceased, meals and gifts are then bestowed upon the monks.

Thai medical students are described as entering into a relationship with their *ajarn yai* that is in the familiar teacher-student model they have known since they were young. The students always refer to the bodies as *ajarn*



Gilded Thai medical diagram of the human body from a pressure massage manuscript from the early 1800s.



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yai, and never as *sop*, the Thai word for cadaver. They sometimes bring flowers to the bodies, greet them with traditional bows, and pray for their *ajarn yai* at the temples. In contrast to the American tendency to depersonalize the cadavers with anonymity, covered hands and faces, humor, even rationalization given the inanimate nature of the bodies, anatomy classes in Thailand post on each dissecting table the name, age, and cause of death of each donor. Students are expected to know the name of their donor when asked, and to retain memory of the name as they practice medicine.

This intimacy yields situations which would be unheard of in Western medical schools. For instance, at the Dalhousie University Faculty of Medicine in Nova Scotia, an introduction is given prior to beginning dissection, advising students to notify the faculty if they know of a recent donor or have recently experienced the death of someone close to them. Any potentially familiar donor is removed, and in the case of a recent death, the faculty ensures that the student dissect a body that is a different sex and age than the deceased relative or friend. In contrast, the *Journal* paper recounts that the grandfather of one Thai medical student had specifically requested that she dissect his body after he died. "She did so," the paper reads, "and was thought to have especially good support from his spirit thereafter."

For each of the donors and the medical students in Thailand, the semester culminates in a ritual procession. Buddhist monks lead the students, who carry the bodies of their dissected teachers to the crematorium.

Buddhism itself may help establish this emotional closeness of students with their deceased teachers. Rather than think of themselves as distinct from the bodies they dissect, students in a Buddhist culture may be encouraged to contemplate the fact that their own bodies will eventually be no different from their cadavers.

The Buddhist Sutra *The Foundation of Mindfulness* has in it a section titled *The Nine Cemetery Contemplations* in which monks are encouraged to view their own bodies on an inevitable continuum which ends with an unpretty vision of decomposition. "And further," reads an English trans-

"She was thought to have especially good support from his spirit thereafter."

lation of one of the *Contemplations*, "if a monk sees a body thrown into the charnel ground, and reduced to a skeleton, blood-besmeared and without flesh, held together by tendons...he then applies this perception to his own body thus: 'Verily, also my own body is of the same nature; such it will become and will not escape it.'" The Buddhist teacher Thich Nhat Hanh refers to this Sutra as the "meditation on the corpse" and suggests that even lay followers of meditation and mindfulness ... [m]editate on the decomposition of the body, how the body bloats and turns violet, how it is eaten by worms until only bits of blood and flesh still cling to the bones, meditate up to the point where only white bones remain, which in turn are slowly worn away and turn into dust. Meditate like that, knowing that your own body will undergo the same process. Meditate on the corpse until you are calm and at peace, until your mind and heart are light and tranquil and a smile appears on your face. Thus, by overcoming revulsion and fear, life will be seen as infinitely precious, every second of it worth living. □

**Christine Montross MD'06** is in her first year of Brown's psychiatry residency program at Butler Hospital.



BY EILEEN O'GARA-KURTIS PHOTOGRAPHS BY KAREN PHILIPPI

# Looking Autism in the Eye

IT'S THE WEEK AFTER LABOR DAY, AND child psychologist Rowland Barrett is already booked until Christmas. So is child neurologist David Mandelbaum.

Barrett, an associate professor of psychiatry and human behavior, heads Bradley Hospital's Center for Autism and Developmental Disabilities.

Mandelbaum, a professor of clinical neurosciences and pediatrics, directs the new, multidisciplinary Children's Neurodevelopment Center (CNDC) at Hasbro Children's Hospital, the pediatric division of Rhode Island Hospital.

The centers offer two of many entry points into the often Byzantine system of health and educational services intended for children with autism.

## THE FIRST HURDLE IS GETTING THERE

THE BRADLEY HOSPITAL CENTER IS ONE OF ONLY three in the nation that share a combination of academic mission, services for children who have both autism and a dual-diagnosed psychiatric illness, and a seamless provision of multidisciplinary services across treatment settings, from home to hospital. It draws referrals from as far away as Alaska.

The CNDC at Hasbro Children's Hospital, flooded with referrals since it opened in January 2006, schedules

Brown faculty work to crack the code for kids trapped in a mysterious realm of the mind

Seven-year-old Bailey Robertson was diagnosed with autism before his second birthday.







"I gave myself one day  
to cry."

children for evaluations by appropriate clinicians—such as neurologists or developmental pediatricians—based on information provided by parents and referring pediatricians. If the parent chooses, the child can then be treated in the center's multidisciplinary clinics.

Where a child is evaluated can be a matter of access, says Mandelbaum. More and more children are being referred for screening, and clinicians are working hard to keep up with demand. "There's usually a two- to three-month wait. If they can get in to see a psychiatrist, they see a psychiatrist. If they can get in to see a neurologist, they see a neurologist."

#### A SPECTRUM PAINTED IN SHADES OF GRAY

"FROM A CLINICAL POINT OF VIEW, IT'S exasperating. It's hard to explain, hard to treat ... I can't point to a lesion and say *There's the problem*," says Mandelbaum. "On the other hand, from an intellectual and scientific point of view, it's fascinating. A child might have a perfectly normal sensory motor exam, and yet have such an incredible, mind-boggling deficit in this other domain. They are very selectively impaired. What does that say about

the specificity of brain function?"

"This is a devastating disease that, at its worst, takes away the very essence of human interaction," he continues. "What must it be like to be the mother of a child who gaze-averts? It cuts to the core of the human condition."

The arc of the autism spectrum—composed of five distinct neurodevelopmental disorders—is long and wide and colored in shades of gray.

Autism spectrum disorders reside at the intersection of neurology, developmental pediatrics, and psychiatry. Broadly defined, the five disorders on the spectrum are characterized by impairment in communication skills, social interaction, and restricted, repetitive, and stereotyped patterns of behavior. But every child exhibits those signs in different combinations and in varying degrees of intensity. (Mandelbaum's research shows an association between IQ level and the severity of *stereotypies*, the repetitive behaviors shared by children with autism.)

There are children with autism who don't make eye contact. Who don't speak. Who can't be touched. Who are compelled to flap their arms furiously,

like flightless sparrows. Who are stung by sounds that others cannot hear.

There are teenagers with Asperger's syndrome who don't have friends. Who lack the social skills to perceive the teasing of classmates, and might not care if they knew. Who excel in the logical world of academics but flail in the murky waters of human interaction.

And there are others who function well ... but have to work painfully hard for what their peers take for granted.

#### WHAT IS IT?

FOUR TIMES MORE COMMON IN BOYS, autism tends to run in families. If one identical twin has it, the other's risk is significantly increased. These factors have long pointed to the genome—and, in October 2006, an international research team for the first time identified a specific gene variant that, when inherited from both parents, more than doubles a child's odds of developing autism.

The jury is out on environmental triggers. Although many in the clinical and epidemiological communities reject the notion, many parents believe that something in their children's immunizations—the mercury-based preservative thimerosal, perhaps, or the combination of the measles, mumps, and rubella vaccines in one inoculation—either caused the condition or sparked a dormant genetic predisposition. Others wonder if something in the prenatal environment causes a child to be born with autism.

Over the past decade, new technologies such as functional MRI, which generates images of brain activity as well as structure, have begun to offer clues. A rising tide of evidence suggests that there are discrete differences in the functioning of neural pathways in the brains of people with autism, as well as the way they use their brains—for instance, processing faces using the part of the brain that people without autism use to process objects.

As guests  
enjoy ice cream  
at his seventh  
birthday party,  
Bailey reacts to  
a song played  
on the stereo.





"I never thought I'd leave a room and he would call for me *Mommy, where are you?*"

Research has also begun to flag differences in the functioning of mirror neurons—which fire both when a person performs an action and when he or she observes the same action performed by another—in people with autism. Does a deficit in this activity explain autism's stranglehold on its victims' inability to empathize and connect with others? Does the deficit give rise to autism? Or does autism—stemming from some other, unknown cause—impair mirror neurons?

"We don't know," says Barrett. "We don't know what autism is. We only know what it looks like."

#### BAILEY'S TEAM

SOMETIMES IT LOOKS LIKE BAILEY Robertson.

Bailey is 7 years old. He's in first grade. He has perfect pitch. He can play the keyboard by ear. And when he is able to construct and articulate a sentence like *Mommy, I want juice*, his 5-year-old brother Spencer leads the cheering section.

At first, Sammi and Doug Robertson feared that their second child was deaf. At 12 months, he wasn't verbal, didn't make eye contact, and didn't seem to notice when they spoke to him.

"He was different," Sammi remembers. "But all of your children are different. And he was my first boy, so I had no point of comparison."

By 15 months, they knew something was wrong. After tests determined that Bailey's hearing was normal, the Robertsons' pediatrician referred them to Assistant Professor of Psychiatry and Human Behavior Stephen Sheinkopf, a clinician at Bradley Hospital and Women & Infants Hospital and a researcher at the Brown Center for the Study of Children at Risk.

In June 2001, at 20 months, Bailey was diagnosed with classical autism.

"We could tell [Dr. Sheinkopf] was so

heartbroken. I was crying. Doug was expressionless. And then we were just numb."

Sammi and Doug went home to North Attleboro and began to carve out a future for Bailey. Three months later, he was receiving intensive in-home therapy through Massachusetts' Early Intervention Program.

But even before her child started treatment, Sammi Robertson had been reborn as a parent activist.

On a rare night out with Doug's parents at a local restaurant, she had picked up a brochure for the National Alliance for Autism Research's first New England "Walk FAR for NAAR" fundraiser. They decided to walk—and to invite friends and family to join "Bailey's Team."

The first fundraising letter went out on September 7, 2001. Despite the philanthropic maelstrom following the terrorist attacks four days later, the letter generated \$8,700 in donations to NAAR, which merged with the national advocacy group Autism Speaks earlier this year.

Over the past five years, Sammi has poured her heart out in powerful solicitation letters. She has chaired three walks for NAAR. And—through golf tournaments, walkathons, and private donations—Bailey's Team has raised more than \$250,000 for autism research.

Sammi was recently awarded NAAR's prestigious London Award—named for Eric London and Karen Margulis London '76 (*see sidebar*)—for her work.

The Robertsons have channeled their energies toward research that they believe will benefit Bailey someday, and will likely benefit future generations.

"You have to believe in something," says Sammi, her voice sinking to a desperate whisper. "Hope is absolutely necessary. Otherwise, what ... is it over? [Research] can take such a long time. But we'll figure it out. We have to. My kids' children will be at risk."

#### CRACKING THE CODE

FIVE YEARS AFTER HE DIAGNOSED Bailey Robertson, Stephen Sheinkopf is watching another small boy in hopes of understanding the physiological aspects of autism.

In a quiet cocoon of a room within the thick brick walls of The Foundry, a converted Providence mill complex that is home to the Brown Center for the Study of Children at Risk, the child sits next to his mother. A stranger enters.

Standing at the door, the young woman initiates a friendly conversation with the little boy's mother. She comes closer, still speaking with the parent. She sits down next to the child and begins to talk to him. Then she starts to interact with him in what Sheinkopf's research protocol calls "a friendly but intrusive manner"—sharing a toy, touching him lightly on the arm.

Behind an observation window, Sheinkopf's team follows the interaction and monitors the child's cardiorespiratory activity, as recorded via ECG leads to which he is attached. Their goal: to understand how children with autism react to social stimuli, compared to children without autism.

Heart rate and vagal tone (a measure of respiratory sinus arrhythmia) are known to reflect sympathetic and parasympathetic responses to social events, and vagal tone in particular is thought to be an important component of the human social engagement system. Given that deficits in social interactions are intrinsic to autism spectrum disorders, Sheinkopf believes that illuminating these physiological manifestations of interpersonal interaction can provide powerful insights into the disorders.

Thirty children have participated in the ongoing study to date. Preliminary results indicate that young children with autism may have a higher threshold in responding to social events—that is, they tend to respond later in the course of the



## “At what point are children engaged?”

interaction—but do not necessarily have a negative response to social stimuli.

“Even though children with autism are much less likely to respond to and interact with others, our findings suggest that by ramping up the intensity of interaction—in a friendly but intrusive way—we can help children to be more responsive to and more engaged with others,” says Sheinkopf.

The study also seems to highlight the variability of autism from individual to individual, as the degree of reactivity during the staged “intrusive stranger” interaction seems to correspond with the child’s observed social behavioral skills.

“People with autism aren’t necessarily totally unresponsive to other people,” says Sheinkopf. “Knowing that could have dramatic implications for treatment and intervention.”

### REDEFINING “HAPPY”

AS A TODDLER, LISA LANDRY’S SON Angelo loved to open and close doors. He didn’t really care if anyone came in. He just liked the opening and the closing. He also liked climbing up and down stairs and turning light switches on and off.

“But he was really smart,” Lisa says. “I told myself I had some kind of quirky genius.”

At 18 months, Angelo knew the entire alphabet and could count to thirty. He was a master at puzzles and blocks. Yet, in play groups he always chose to play alone. Often—despite his precocious command of language—he could not communicate. And he would not look into his mother’s eyes.

Lisa had known from the beginning that there was something different about Angelo. He was 6 months old before he slept through the night. He cried constantly. And he didn’t like to be held.

It was a friend’s offhand comment at a birthday party—“He’d make a great door-man”—that sparked Lisa’s *A-ha* moment. *Others could see it too.*



After opening his birthday gifts, Bailey takes a short break from the party.

When Angelo was two, Lisa took him to the early intervention program at Family Resources in Woonsocket for evaluation. “They didn’t say the A word to me,” she recalls. Told that Angelo was at risk for sensory integration disorder, she took him to the Groden Center in Providence for play therapy.

Six months later, she had him re-evaluated at Hasbro Children’s Hospital. This time, the A word was spoken—with an additional descriptor. Angelo had Asperger’s syndrome.

“I gave myself one day to cry,” Lisa remembers. Then she got busy.

An attorney in private practice, she closed her office and started working as a hospital-based advocate for the Rhode Island Parent Information Network. That work segued into her current full-time position as a parent advocate and coordinator at the hospital’s Child Neurodevelopment Center, where she serves as friend, educator, and champion of parents of children with special needs.

“I love the work,” she says. “When you help others, it’s healing.”

Angelo is now in kindergarten. Exhibiting the laser-like focus common to children with Asperger’s, he is very into the solar system, clocks, and weather.

And—thanks largely to early intervention starting at the age of two, his mother believes—he’s making progress.

He’s able to recognize signs of distress in himself and ask for help. He recently invited a friend home for a play date. “And one day,” says Lisa, “he hugged me and told me that he loved me. And he made direct eye contact.”

It’s those moments—the small, incremental victories—that get her through the day, she says.

Sammi Robertson agrees. “You learn to re-evaluate what makes you happy.”

### WHAT ABOUT THE SIBLINGS?

ISABELLA LANDRY WAS FOUR WHEN HER brother, Angelo, was diagnosed with autism. Rachel Robertson was the same age when Bailey was diagnosed. The youngest Robertson child, Spencer, was an infant. (Sammi and Doug watched him closely for years, until it was clear that he did not have autism.)

“Rachel lost out on a lot of stuff,” Sammi acknowledges with regret. “There were no play dates. Bailey was in therapy constantly. He didn’t sleep through the night for two years. I try to make up for things, without spoiling her ... but the reality is that it’s been hard.



“Perhaps someday research will help us to improve our lives...this is all I have to hope for and believe in.”

“Rachel appreciates how adorable her brothers are, though, and she likes to help me take care of them,” she continues. “And Spencer and Bailey have a really special relationship. [Even though he still has trouble making eye contact] Bailey will run up to Spencer, look him intensely in the eye, and run away. That’s how he engages. That’s how he says *Let’s play*.”

In fact, Bailey’s little brother seems to have intuitively worked out one of the key findings of Sheinkopf’s research. “Spencer is really intrusive with him—in a good way. It’s like he just doesn’t accept Bailey’s limitations.”

The experience of being connected to Bailey has given her other children a unique gift, Sammi says. “In that sense, it’s been positive. I think it’s sensitized them to special people.”

It’s a common phenomenon among siblings of special needs children, says Associate Professor of Psychiatry and Human Behavior Debra Lobato.

“Research has shown that about 50 percent of kids who have a sibling with a developmental disability later report that they learned a lot from the experience, often saying that it was the most meaningful thing in their childhood.”

A researcher at the Bradley-Hasbro Research Center, a collaborative program of Bradley Hospital and Hasbro Children’s Hospital, Lobato also directs the SibLink program at Hasbro. SibLink offers a menu of programs for siblings of children diagnosed with chronic medical, developmental, or behavioral problems—from evaluation, to individual and family counseling, to group workshops.

“The correlation between knowledge and adjustment is very high [among siblings of children with autism],” says Lobato. “We work on helping kids learn about their siblings’ disability, trying to help them not to feel so isolated. Often, we hear *I can’t relate to other people* [who don’t have autism in their lives].

A key determinant of good adjustment among siblings is the mental health of parents—especially mothers—and some degree of personalized parental attention. That can be a tall order for families struggling to care for a child who has a devastating neurological disorder.

“A lot of times what’s left behind [for siblings] is a parent who’s kind of burned out,” says Lobato. “One thing that helps is establishing special rituals with the healthy kids—something as simple as



At the end of a long day, Bailey relaxes with his father.



# Transforming Pain into Possibility

**IN 1989**, WHEN TWO-YEAR-OLD ZACHARY LONDON WAS DIAGNOSED WITH autism, there were few resources available. There was no Internet. There were no high-profile advocacy groups. And there was very little research.

Karen Margulis London '76 gave birth to Zachary's sister, Rachel, two days after she and her husband, Dr. Eric London, received the diagnosis. Five years later, they launched the National Alliance for Autism Research (NAAR.)

"I don't want to make it seem like Zachary was diagnosed and we ran right out and started a national charity," she says. "Initially our focus was to do intensive therapy with Zachary, find the best school we could for him and keep a very close eye on Rachel's development. But the whole time we were also looking for information and trying to talk to anyone who was doing autism research. It was becoming increasingly clear that there wasn't much going on."

In early 1994, Karen and Eric had dinner with Harvard-based autism researcher Dr. Margaret Bauman and asked her if there was an advocacy organization in the U.S. focused solely on autism research. She said that there was not—but that such an organization would be critical to building momentum in the field.

"The next day we were at a conference at which she was speaking, and someone in the audience asked her the same question. She pointed to Eric, indicating that he was starting such an organization. He was immediately surrounded by dozens of other parents. There was no going back after that."

Karen's next call was to her Brown roommate and best friend, Susan Hyman '76 MD'79. Ironically, Susan—a developmental pediatrician then at the University of Maryland—was an expert in autism spectrum disorders. Susan helped recruit a dream team of top scientists to serve on NAAR's Scientific Advisory Board. Karen, a corporate attorney, organized the new nonprofit and started fundraising. Eric, a psychiatrist, focused on the scientific and clinical aspects of the enterprise.

Together, they launched the first autism research charity in the nation from the basement of the Londons' home in suburban New Jersey.

Over the next ten years, NAAR awarded more than \$30 million in grants to 270 autism researchers worldwide—including Stephen Sheinkopf—and sparked an explosion of interest in the field.

In February 2006, NAAR merged with Autism Speaks, a vibrant new advocacy organization launched by NBC Universal CEO Bob Wright and his wife, Suzanne, who have a young grandson with autism.

Eric London and Susan Hyman continue in leadership roles at Autism Speaks. Karen is now in the early stages of establishing her next venture. Global Communities of Support aims to create quality, replicable vocational opportunities and supported residences for teenagers and adults with autism as they "age out" of the school system.

"These were once 'throw away' children who often lived their entire lives in institutions," says Karen. "Now, for the first time, autistic children who have had the benefit of teaching and training are becoming adults—but without the support mechanisms critical to sustaining their hard-won accomplishments. For those who love them—but will not always be around to protect them—this must be our next great effort."

NAAR founders  
Karen Margulis  
London '76 and  
Dr. Eric  
London put  
autism research  
on the map.

five basketballs shoots every night, or a pretend tea party every afternoon."

Research has shown that psychiatric and neurodevelopmental illnesses are more difficult for siblings to cope with than somatic illnesses, even cancer, she adds. "Disorders that are disruptive to routine in the home are the hardest."

Lobato and Wendy Plante, associate director of the SibLink program, are currently analyzing data from a just-completed study that compared adjustment levels among siblings of children with autism and siblings of children with diabetes—measuring a set of behavioral and somatic symptoms of anxiety.

One preliminary finding: the children in the autism cohort showed more somatic complaints, such as headache and stomach ache, as well as more behavioral disruptions, than the diabetes cohort.

## ONE CHILD AT A TIME

PARENTS AND SIBLINGS ARE FRONT AND center in the world of Karyn Blane.

Blane and M. Christopher Borden, both assistant clinical professors of psychiatry and human behavior, co-direct Bradley Hospital's Intensive Behavioral Therapy (IBT) program, which brings up to 40 hours a week of focused, one-on-one therapy, beginning before the age of four, to kids who have been diagnosed with an autism spectrum disorder.

"Sometimes the kids we work with are part of the family, but at the same time not part of the family," she says. "In those cases, we look for qualitative gains, like sitting down for dinner with the family, or reading a book with mom ... modifying behavior in order to develop more everyday relationships."

She and her colleagues incorporate siblings, who are usually eager to participate, into their work—asking them to model appropriate behavior, for instance. And parent involvement is critical. "Parents are so in tune with their kids' needs. We really seek to form a partnership with the family.



“There’s nothing like seeing another kid in the room who shares your experience.”

Substantial gains can be made when everybody’s on the same page.”

Blane and Borden’s team collects data on each step in a child’s treatment and then meets with the family biweekly. Sometimes goals and gains are modest. And sometimes progress is astonishing. “We’ve seen kids make tremendous gains ... even kids who are more impaired when we meet them learn how to communicate and function in classrooms.”

Almost all of the children in the IBT program participate in school programs, their curricula guided by Individualized Education Plans (IEPs) tailored to their needs. And only a fraction of them ever need inpatient care at Bradley. In fact, the program’s outcomes data reveal a dramatic overall success rate.

“Nationally, about 14 percent of children with autism require out-of-home placement by the time they’re 15,” says Barrett. “Only 1 percent of kids who’ve gone through our IBT program have needed to be placed out of the home.”

Due to capacity issues, only 25 children can participate in the IBT program at any one time. The wait can be anywhere from a few months up to two years.

The IBT program is part of a continuum of services the Bradley Hospital Center for Autism and Developmental Disabilities provides at home, in school, in the community, in an outpatient specialty clinic at the hospital, and, on rare occasions, on an inpatient basis. The multidisciplinary team of professionals—psychiatrists, psychologists, occupational therapists, psychiatric nurses, and others—follow the child across settings, providing the comfort and clinical benefits of continuity.

“Ours is the largest, most comprehensive program in the region,” says Barrett. “[Our center] treats more kids in one week than Bradley Hospital treats all year in its inpatient program.”

#### IS AUTISM EPIDEMIC?

IT HAS BEEN ESTIMATED THAT ONE IN every 166 American children has an autism spectrum disorder—a tenfold increase in incidence since 1991. Is it a quiet epidemic?

It’s a controversial question, and no one knows for sure. Barrett and Mandelbaum believe that a reassignment of diagnosis accounts for the increase. Both

independently cite a California study, published in *Pediatrics*, showing a decrease in mental retardation that virtually mirrors the increase in autism—suggesting that the higher incidence of autism actually signals improvement in accuracy of diagnosis. Pointing out that Asperger’s syndrome was not included in the Diagnostic and Statistical Manual of Mental Disorders (DSM) until 1994, Barrett also asserts that the resulting extension of the autism “spectrum” has had a significant impact on incidence.

A recent Johns Hopkins study, published in *The Journal of Developmental and Behavioral Pediatrics*, reported that more than 70 percent of Atlanta-area pediatricians also attribute the increase to changes in diagnostic criteria and treatment.

Regardless of the source of the increase, Barrett is sharply aware of the growing need for services. “We continue to work hard with the children in our care, using all of the resources available to us ... but the reality is that, by and large, families [of children with autism] are grossly underserved.”

For NAAR co-founder Karen Margulis London ’76, it’s clear that the answer lies not only in clinical excellence, but in medical research that will eventually identify cause and cure.

“My son is now 19 years old and he’s been in an exceptional school since he’s been 2½—a school that was established 36 years ago by a family who sought to create an educational environment for children then thought to be uneducable,” says London. “My family has been incredibly fortunate to benefit from their advocacy and now it’s our turn. This generation’s imperative is to advance research.” □

**Eileen O’Gara-Kurtis** is the founder and president of Silver Branch Communications based in Seekonk, MA. She is a frequent contributor to Brown Medicine.



Bailey leans on his mother for support.



Sivan and Jeff Hines  
at home in Atlanta with  
their son, Matthew.  
Their daughter, Renuka,  
is a junior at Columbia  
University.







MICHAEL SCHWARZ

# Two Doctors in the House

BY DAVID  
TREADWELL

The occupational hazards  
and surprising rewards of  
being a dual-MD couple

SOME COUPLES START OUT AS HIGH SCHOOL SWEETHEARTS. OTHERS meet in college. Some even get to know each other in medical school, as they dissect a cadaver in anatomy class or learn to take a history.

While it might sound romantic that some Brown Med alumni end up married, the potential pitfalls facing a dual-MD partnership are real. In an editorial in a 1994 issue of *British Medical Journal* Claire Beiser, assistant professor of medicine at the University of Maryland School of Medicine, noted that strong personalities, competitiveness, differing priorities, and time pressures are more or less part and parcel of such relationships. She concluded that “the challenges and barriers are great, and individuals, couples, and the profession must appreciate them.”

To be sure, some specialties carry with them more perils than others. A

1997 study of medical specialty and incidence of divorce published in the *New England Journal of Medicine* found that, while the divorce rate of physicians over a 30-year period was close to the national figure, surgeons and psychiatrists were especially at risk, dissolving their marriages much more frequently than other MDs or the general public.

Despite the drawbacks, however, it seems that coping with the unique challenges of being married to a physician while also *being* a physician can actually strengthen the bond. Doctors wedded to doctors have to communicate about critical issues—work versus family, division



of domestic labor—and that alone often helps bring two people together. In fact, a 1999 Case Western Reserve University study published in the *Annals of Internal Medicine* noted that more and more physicians are finding spouses within their profession. And though they earn less individually and work fewer hours, they spend more time on the home front and tend not to value one spouse's career over the other. "Overall," said Susan Hinze, associate professor of sociology at Case Western and a study author, "dual-doctor marriages have a better life and more contentment."

But just how do two Type A personalities keep a marriage alive against the constant pull of on-call time and patient needs and domestic duties and, for many, enormous educational debt? And where do children fit into the picture?

The four Brown Med couples below experience first hand, every day, the trials and rewards of doctor-doctor relationships. The words "sharing" and "journey" came up repeatedly during conversations, and it might be said that medical marriages are journeys to the extreme, with constantly changing cultures and curren-

"We met during our rotations in medical school—first ob-gyn, then pediatrics, and surgery. We were the only ones in ob-gyn who hadn't yet done our surgical rotation and I remember admitting to each other that we hadn't yet learned how to tie knots."

Before they tied the marriage knot, Melissa and John had to endure time away from each other during one of the toughest challenges for all doctors: residency training. "We didn't sign up for a 'couples match' for our residencies, so I ended up in New Haven and John landed in Rochester—six hours apart. I remember driving through this horrible snowstorm to meet him halfway in Amsterdam, New York, and wondering if I should turn back and thinking, 'No, if I don't see him this weekend, I won't see him for another two months.'"

John's memories of finding time to get together are equally harrowing. "One



Joanne  
Silvia  
and Paul  
George

return to deliver her baby if needed. Non-doctor couples don't need pagers!"

Nor are non-doctor couples likely to celebrate special occasions in the hospital cafeteria, where Joanne and Paul shared their second anniversary meal.

Young dual-doctor couples face another potential burden: enormous educational debt. Paul considers himself fortunate on that front.

"We know some couples who owe about \$250,000. Thankfully, our combined debt is considerably less."

In spite of the strains that their residencies impose, Paul would have it no other way. "I miss Joanne when I'm not with her. She's my best friend."

## Housework and Homework

WITH ALL THE TIME DEMANDS INHERENT in the profession, it's imperative that couples strike the right balance between work responsibilities and personal needs.

**"If you can survive your residencies, then you know things will get better."**

cies, testing the spirit and character of even the most adventurous travelers.

## The Rigors of Residency

"IF YOU CAN SURVIVE YOUR RESIDENCIES," says Sivan Hines '84 MD'87, a pediatrician in a group private practice near Atlanta, "then you know things will get better."

Melissa Gaitanis '92 MD'96, assistant professor of medicine at Brown Medical School, recalls the first time she encountered her husband-to-be, John Gaitanis MD'96, assistant professor of clinical neuroscience at the Medical School:

time I drove all the way down to New Haven to see Melissa after being up for 36 straight hours. It was crazy."

Joanne Silvia '00 MD'04, a third-year resident in family medicine at Memorial Hospital of Rhode Island, and husband Paul George '01 MD'05, in his second year of family medicine residency at Memorial, are currently in survival mode, each working 60 to 70 hours a week. Medicine can intrude even on their vacation time, according to Paul. "We just returned from a vacation to Coopers-town, New York, and Joanne had to take along her pager, because she had promised one of her patients that she would

Moreover, each partner must be willing, both men and women noted, to divide up domestic duties.

Robert George II '73 MD'77, a family physician in private practice in Mercersburg, PA, helps with the shopping and the cooking. "You have to learn how to share," he says. "I tended to do the cooking, as Elizabeth often came home later, after delivering a baby or something. She did the gardening and clothes shopping and helped the kids with the homework. I was better at driving the kids to activities, getting them from place to place. She planned vacations; I went along and made sure that things worked."

COURTESY GEORGE AND SILVIA



"Bob's a quicker and more efficient cook," admits his wife, Elizabeth George '73 MD'76, also an internist in private practice, "so it works out well."

She adds that sharing time away from the daily grind is also extremely important. "Early on in our practice, we always blocked out time to go away with the family several weeks a year. Our patients appreciated a little bit of forewarning

especially for doctors in pressure-cooker, time-demanding professions. "Be flexible," cautions Sivan. "You can't put your career above everything else. You have to decide together what you want as a family."

"We regularly schedule 'date nights' or three-day weekends, time away with each other when we're not at meetings," says her husband, Jeff Hines '83 MD'86,

allocate quality time with their kids. When their three children (two of them Brown alumni from the Class of 2002) were young, Bob and Elizabeth worked out an arrangement in which they both worked two-thirds time so that one of them would always be there when the kids got home from school.

Melissa, too, has cut back her work responsibilities by 20 percent to spend

### "I miss Joanne when I'm not with her. She's my best friend."

that we were going away, and they were very understanding that their family doctors were taking time off to be with their family. Sounds simple, but some doc couples just aren't careful to plan the time away."

"We try never to be on call at the same time," says Melissa, "so we can share responsibilities for our kids." She takes care of the kids if John is scheduled to make a presentation the next day—and vice versa.

Priorities matter for all couples, but

attending gynecologic oncologist with Southeastern Gynecologic Oncology, LLC, and associate clinical professor in the Division of Gynecologic Oncology at Morehouse School of Medicine in Atlanta.

The Gaitanises know where their priorities lie, according to John: "We both value family most. We would sacrifice our careers for our family."

The three couples with children—all but Joanne and Paul, who plan to have kids "some day"—stressed the need to

more time with their 4-year-old son and 2-year-old daughter. "With medicine you can be flexible and adjust your schedule up or down."

Jeff and Sivan have always insisted on carving out time for their two children. "I wanted to be a young dad when I had energy," says Jeff. "I wanted to be involved in their lives when they were growing up. We've done a lot together as a family, and we have always tried to share a family sit-down dinner when we can talk about the children's day."

The Hineses remain very involved in their children's lives. They often fly from Atlanta to New York City to see their daughter, Renuka, a dance major at Columbia, perform. And Jeff gives haircuts to his son Matthew, a high school sophomore, as a way of keeping the communication lines open. "Sometimes he'll grumble about my bringing up subjects like girls and relationships while I'm giving him a haircut, but I say, 'That's what happens when you get a haircut from me.'"

### They Just Get It

MARRIAGE IS A BIG DEAL, AND BEING married to someone with a career as demanding as one's own can seem like an even bigger deal. But this concern did not factor into the planning of these four couples.

Over and over, the eight individuals in these four relationships said, *He knows*

SCOTT KINGSLEY



The Doctors Gaitanis relax at home with their children, Sophia and Nicholas.



Liz and Bob George in 1973 following their wedding in Manning Chapel. Father Howard O'Shea officiated and Professor William Dinneen played the organ.



*what it's like or She identifies with what I'm going through.*

"We each understand when the other person doesn't get home on time or doesn't have time to call," says Joanne. "We don't get upset if the other person comes home exhausted or too tired to go out."

Paul agrees. "We can relate 100 per-

cent to what the other one is dealing with. We can share with each other and decompress from the day—or night. And because of the long, strenuous work hours, we cherish the time that we're together."

"It can be challenging with two driven people living together," admits Bob, "but it's no harder than, say, being a father or a mother."

Elizabeth is even more emphatic: "Being a female physician, I can't imagine *not* being married to a doctor."

What about bringing work home at

night? What about living with a person who, like you, is all about healing people? Wouldn't it be easier to be married to someone with completely different demands?

Not according to Bob. "We really never leave medicine," he says. "We're always talking about patients or ideas and concepts. And, of course, the media are

always filled with medical stories, which have implications for our practice or our patients. The truth is that most doctors don't talk about anything but medicine, so in our case it's naturally part of the conversation."

"Married doctors share the daily joys and horrors of medicine, all the stories," says Sivan. "Jeff and I have separate practices and specialties, but sometimes our patients overlap. I have an instant relationship with someone my husband has served. And it's wonderful to see how much he is respected."

It can even help to have an MD partner. "When a patient calls at 3 a.m. and has a question about infectious diseases," says John, "then I can just turn around and ask Melissa, because that's her specialty."

Elizabeth agrees—but is quick to add, "It's great when the phone rings in the middle of the night and the person calling is Bob's patient, not mine."

In the end perhaps it's the person, not the profession, that counts.

"Marrying a doctor was never an issue for us," says John. "The personal connection would have been there even if we had been plumbers. We started out as good friends and evolved into marriage."

"Sivan is still my best friend," says Jeff. He remembers being taken with the woman who was to become his bride during their first encounter at a meet-the-professor mixer at Brown. "I love her as much as the day I met her."

Reflecting on their years together, Sivan shares Jeff's enthusiasm. "If I'd known when I first met Jeff what I know now, I would have been even more excited. We are blessed."

John likens his changing marriage to an ongoing adventure. "We connected first as students, and we've grown in

friendship and evolved in our marriage. Medicine is really a unique journey: pre-med courses, medical school, residencies, practice. We've faced different challenges at each stage, but we've faced them together." □

**David Treadwell** is a freelance writer living in Brunswick, ME.

*This small sample of alumni couples was chosen for range in age, geography, specialty, and availability. Brown Medicine welcomes stories and feedback from other alumni couples of all kinds.*

COURTESY GEORGES



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**YOU'VE DONE IT, AGAIN!** Brown Medical School alumni, parents, students, University alumni, faculty, and friends led the Brown Medical School Annual Fund (BMSAF) to another record-breaking year. Donors to the BMSAF gave \$636,144, surpassing the goal of \$600,000. Donor participation reached new heights as well, with 1,166 individuals making gifts—a 25 percent increase over last year.

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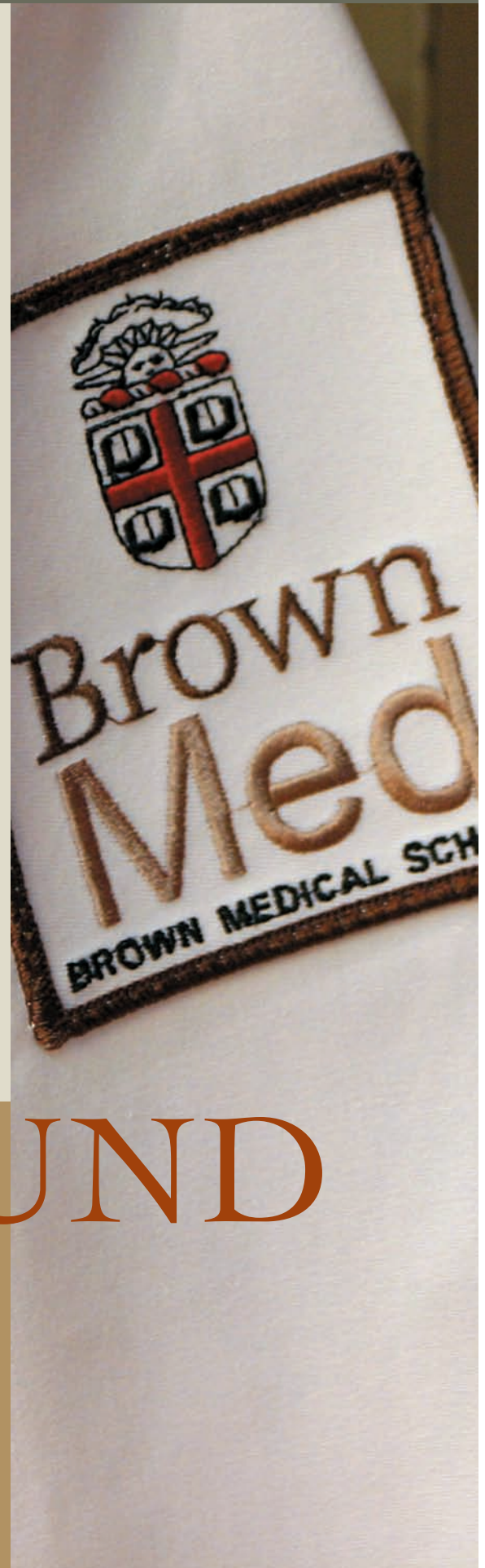
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Parents of Brown medical students outdid themselves this year in supporting the Brown Medical School Annual Fund (BMSAF). The number of parents participating in giving was up by 16 percent, resulting in a 30 percent increase in dollars. We are incredibly grateful to all parents, who, in addition to offering their emotional and financial support to their medical students, are showing their support for Brown Medical School by giving to the BMSAF.

Part of this year's success can be attributed to the efforts of the Medical Parents Committee (MPC). The MPC offers parents of PLME and medical students a great opportunity to become more involved in Brown Medical School. Last year, the MPC, led by Saberah and Tariq Malik P'01MD'06, took on a greater role in fundraising for the BMSAF. We thank the Maliks for their hard work.



Joan and George Turini P'05MD'09 (pictured above with Dean Eli Y. Adashi) are beginning their term as chairs of the Medical Parents Committee this fall. They will continue the fundraising work of the MPC and its other activities, such as acting as ambassadors for the Medical School through involvement in hosting events or students (when they travel for residency interviews), and planning parent programs.

If you are interested in learning more about the MPC, please contact Parent Programming at Med\_Parent@brown.edu or 401 863-3232.

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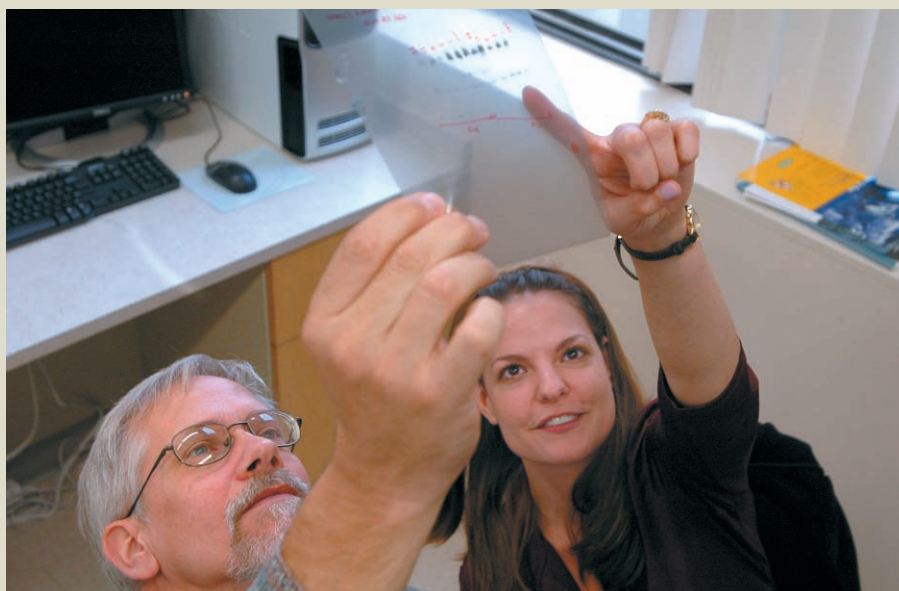
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In addition to being given biographical information about the students receiving their scholarships, donors are invited to the annual scholarship dinner, where they have the opportunity to meet their students. Term scholarships offer top donors to the BMSAF a new level of connection and involvement with the students who benefit from their support.

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LUCAS FOGLIA



## DEVELOPMENT

# Brown Med Alumna Gives Back

MEDICAL STUDENT SCHOLARSHIPS RECENTLY RECEIVED A SHOT IN the arm from the largest gift to Brown Medical School from one of its alumni. In honor of her 30th reunion, Marilyn Dawson Sarles MD'76 committed \$1 million to establish the Sarles Scholarship Fund for Medical Education.

Dr. Sarles says "her loyalty to Brown and Dean Adashi's demonstrated commitment to academic excellence" inspired her to make this gift, with the intent of furthering the education of future generations of talented physicians.

After completing her residency training at Roger Williams Medical Center in internal medicine, Dr. Sarles served as an emergency medicine physician in that hospital for a number of years. She and her husband, H. Jay Sarles, currently reside in Wellesley, MA. Their daughter Liz is enrolled in the master's degree program in Brown's Department of History, while daughter Katie is taking post-baccalaureate courses at Tufts University with the goal of becoming a veterinarian. Their son, Dan, is pursuing an advanced business degree at the University of Texas.

The scholarship also memorializes Jay Sarles's mother, Jaqueline Gage Sarles, a member of the Pembroke College Class of 1935. Jaqueline Sarles was committed to supporting a wide range of educational opportunities, particularly in Barrington, RI.

In addition to establishing the

scholarship fund, Dr. Sarles has been a steadfast supporter of the Brown Medical School Annual Fund. These gifts benefit two of the top priorities of the Campaign for Academic Enrichment, and help ensure that financial support will be in place for Brown medical students for years to come.

— KRIS CAMBRA

Jaqueline Gage  
Sarles '35



Marilyn Dawson  
Sarles. At right,  
with Dean Adashi  
and members  
of the MD classes  
of '76 and '81.





# Alumni Album



Paquette stands at the entrance of the B'aath Party Headquarters in Baghdad. Right, Paquette in surgery at the 10th Combat Support Hospital.



## Alumni Profile | ED PAQUETTE

### A Farewell to Arms

LIEUTENANT COLONEL ED PAQUETTE MD'94 WAS A RARE SORT OF undergraduate: he knew what he wanted to do with his life and had a good idea of how to get there. First he got in with the Early Identification Program at the University of Rhode Island, which grooms select students for a place at Brown Medical School. Then he took up with another crowd, the folks that would finance his medical training. He enrolled in the U.S. Army Health Professions Scholarship Program. "You make a choice when it comes to paying for school," he says. "You either owe the bank, you owe your parents, or you owe the government."

Paquette chose the feds. July 2007 will mark his 13th and final year of military service. And with tours in two of the most contentious international conflicts in recent memory—Bosnia and Iraq, respectively—it's safe to say that Uncle Sam has been paid back in full.

Today, Paquette provides care at the Womack Army Medical Center at Fort Bragg. He and wife, Teresa, live in nearby Fayetteville, NC, with their children—three boys, ages two to six, and a 9-month-old girl born while Paquette was in Iraq. He was called to active duty on the fourth anniversary of the September 11 attacks.

COURTESY PAQUETTE



"I had it easier than most," he says of the experience. "This is why you become a surgeon in the Army, to go to combat and take care of the soldiers. You feel like you're doing something good."

Paquette, a trained urologist, was stationed with the 10th Combat Support Hospital (CSH), a facility that sees traffic comparable to the busiest trauma centers in the States. "Our primary objective was [to care] for the troops. We would patch them up and move them on," he says.

The CSH is embedded in the Green Zone, a four-square-mile enclave surrounded by concrete blast walls, razor wire, and armed checkpoints. The area is home to military personnel, the U.S. and British embassies, and the seat of the Iraqi government. It's also the only place soldiers in the field can look to for R&R. "It's very well fortified," says Paquette. "There are dorm rooms, hot water. A lot of [soldiers] were in the middle of nowhere. They're really out there on these dangerous missions. They come back to the Green Zone and can let their guard down a bit."

When duties called Paquette away from the relative safety of the Green

Marines that come in and are hurt—now they're going to be in the VA system for the next 30 years."

A foot injury brought Paquette back from Baghdad earlier than planned. Today he's preparing for life in medicine minus the army fatigues, a move he made with his family, among other

factors, in mind. "My wife and I have this joke, she says 'You should never marry an army man or a surgeon,' and I'm an army surgeon," he says with a laugh. "But Teresa has always been very supportive. And I'd do it all again if given the chance."

— JUMOKE AKINROLABU

## EYE ON ALUMNI



Dan Harrop

### Doctor Mayor

CLINICAL ASSISTANT PROFESSOR OF Psychiatry and Human Behavior Dan Harrop '76 MD'79 describes Providence Mayor David Cicilline '83 as "honest and ethical." But such praise doesn't mean he won't take his job if given a chance. In November, Harrop will square off against the Democratic incumbent in the race for the City's highest office.

"I'm running at the request of Providence Republican Committee," Harrop says. Though flattered by the recognition of his peers, Harrop waited until the last minute to enter the running. There were several factors to consider—his chances of winning in an overwhelmingly Democratic community chief among them. "Rhode Island is pretty bad, but Providence is the worst," he quips. "The city could benefit from a two-party system." And then there's the competition. "Some don't

like [the mayor's] policies, but he's been active and is very popular. There's also the question of money—you need a reasonable amount to run for office. I wanted to make sure people would back me."

Casting his misgivings aside, Harrop announced his candidacy in June and swept the Republican primary in

Harrop believes his professional background could be just the treatment Providence needs.

September. His platform rests on finance and education reform, both critical issues to Providence. "The city has continually raised property taxes, its pension is under funded, and every public middle school has failed according to No Child Left Behind."

Harrop believes his professional background could be just the treatment Providence needs. "City government is a human service institution. Its concern is the welfare and safety of its citizens—these are the same concerns of physicians," he says. "I'm a psychiatrist and I have an MBA. But working as a physician, dealing with people on a humanist level, has been better training than any business degree." — J.A.

"This is why you become a surgeon in the Army, to take care of soldiers."

Zone, he traveled by convoy with other soldiers, his M-16 assault rifle locked and loaded. "It was a nice show of force I never had to use," he says. "It's the real soldiers that are taking all the risks. Obviously, the worse thing is the trauma and loss of life—women with no legs, kids killed from IED's going off. And then you have these big, strapping

COURTESY HARROP



# Alumni Album

## EYE ON ALUMNI



### SuperBug

MILK DOES A BODY GOOD. BUT IN winter 2006, Bharat Ramratnam '86 MD'93, assistant professor of medicine at Brown, found that it could do even better when curdled into food staples like yogurt and cheese. Each carries

**"The more we study [HIV/AIDS], the trickier it seems to be."**

lactic acid bacteria, a harmless bug that could be the newest ally in the fight against HIV/AIDS transmission.

It all started with cyanovirin, a protein scientists found could block HIV from penetrating the mucous membranes, the entry point of HIV. The

discovery came with a hitch: cyanovirin is unstable—when ingested by mouth, stomach acids dissolve the protein and topical applications produce too brief an action to deliver on its therapeutic promise.

Ramratnam and his team of researchers got creative, genetically engineering lactic acid bacteria to deliver and then mass produce cyanovirin. "Lactic acid bacteria [LAB] naturally lodge on to mucosal surfaces," Ramratnam says. "[HIV] needs to make its way thru the mucosa into the human body. By having LAB produce cyanovirin on mucous membranes, we may have a way to prevent HIV invading the human body."

Ramratnam hopes to formulate the modified bacteria into topical gels or capsules that could be used before sex. And with HIV/AIDS infection at pandemic proportions, the need for new tools to stem the spread of the diseases is at critical mass. "The more we study [HIV/AIDS], the trickier it seems to be," Ramratnam says. "The key is not to give up."

— J.A.

## CLASS NOTES

### 1975

**Mark S. Blumenkranz '72** MMS'76 is chair of the scientific advisory board of MacuSight, Inc., developer of treatments for ocular disease. The FDA recently approved MacuSight's "IND" drug to combat macular degeneration. Phase I of the drug's clinical trial begins later this year.

### 1977

**Clarence "Bud" Wiley '74** MMS'77 wants classmates to know that he is medical director of Beauty Thru Dermatology in Oklahoma City, OK. He is married to Cynthia, and on May 20, 2005, Clarence Wiley Jr. was welcomed to the family. Bud's son, Chris, 27, is a staff sergeant in the Air Force and has a daughter, Joo-Yung, 2, with wife Ju-A. Amber, 25, received her BA from Yale in 2003 and her MA from the University of Virginia in 2005. She is working toward a PhD in architecture from George Washington University. Roland is 15. Bud can be reached at budbud1028@aol.com.

### 1981

**Robert Golomb '78** PRACTICES EMERGENCY medicine at Alta Bates Medical Center in Berkeley, CA. He writes, "I have been an attending physician [here] for 15 years. It is a great place to work. My patients have included Nobel laureates, the former president of the Sierra Club, folks that have lived in the 'People's Park' since the 1860s and everyone in between. I think I am starting to get the hang of this doctor stuff."

### 1982

**Sylvia Gates Carlisle** LIVES IN ELK Grove, CA, with her husband, **David Carlisle** MD'82, her son, David, and



her daughter, Aimee Jeanne. She is an administrator at Health Net of California in Oakland.

## 1985

**Patricia Recupero**, JD, A CLINICAL PROFESSOR of psychiatry and human behavior and CEO of Butler Hospital, took office as the vice president of the American Academy of Psychiatry and the Law (AAPL) at its annual meeting in October. She has been active in the



Patricia Recupero

organization for almost 10 years. She has also been appointed to two different roles for the American Psychiatric Association: chair of the Manfred S. Guttmacher Award Committee and area representative of the Assembly and member of the Assembly Executive Committee for Area I (New England, Ontario, Quebec, and Eastern Canada).

**Scott Haltzman** '82 PUBLISHED HIS first book, *The Secrets of Happily Married Men*, in January 2006, and is working on his next book, *The Secrets of Happily Married Women*, due in bookstores in 2007. Scott lives in Barrington, RI, with his wife, Susan, and two teenagers, Matt and Alena. He

still teaches in the Department of Psychiatry and Human Behavior at Brown. He can be reached at [www.DrScott.com](http://www.DrScott.com).

## 1986

**Joel Kline** '83 IS A PROFESSOR OF medicine and occupational health at the University of Iowa, where he directs the UI Asthma Center. He leads programs in both basic and clinical/translational research, and is not pleased about the reversal in NIH funding levels. He is married to **Catherine Woodman** '81 MD '85, who directs the psychiatry residency. They have four sons, ages 12, 14, 16, and 18. The oldest, Jake, started at Brown this fall. Joel and Cathy moved from Providence to California for their residencies, then to Iowa "just for three years" for Joel's pulmonary/critical care fellowship training. Now they have fallen in love with Iowa City, which has a surprisingly high number of Brown alums, and can't seem to leave.

## 1990

**Linden Hu** '87 AND WIFE SUSIE announce the February 6, 2006, birth of Madeline Hu. She joined her big sister, Amanda, 2. Linden is associate chief for research in the infectious diseases division at Tufts-New England Medical Center and is an associate professor in microbiology and immunology at Tufts University, where he studies Lyme disease. Susie is an assistant professor at Brown in nephrology. They would love to hear from old friends and classmates. Linden can be reached at [LHU@tufts-nemc.org](mailto:LHU@tufts-nemc.org).

## 1993

**Bharat Ramratnam** '86 HAS BEEN awarded a NIAID grant that will deter-

mine the efficacy of siRNA in preventing and/or treating HIV, HSV and HPV in relevant animal models. He writes, "Hopefully, the preclinical data will allow us to justify translating the findings into clinical trials in the future."

## 1997

**Srihari Naidu** '93 HAS BEEN APPOINTED director of the Catheterization Laboratory and of the Interventional Cardiology Fellowship Program at Winthrop University Hospital, a 600-bed tertiary care hospital affiliated with SUNY-Stonybrook Medical School.

**Lindsay E. Phillips** '90 WAS HONORED by the American Academy of Family Physicians Foundation with the 2006 Pfizer Teacher Development Award for her commitment to education in the field of family medicine.

## 1998

**Adda Winkes** '94 MARRIED LCDR TIM Kunkel, USN, on November 4, 2005, in Kailua, HI. **Madhu Ananthakrishnan** MD'98 was in attendance. Adda and Tim want to thank the many family members and friends from Providence who came all the way to Hawaii to celebrate. Adda can be reached at [awinkes@hawaii.rr.com](mailto:awinkes@hawaii.rr.com)

## 1999

**Felix Lui** '95 WRITES, "AFTER A GRUELING year in Baltimore finishing my trauma/surgical fellowship at the Maryland Shock Trauma center, I was glad to move back in with my wife, Lara. There I joined the faculty at Yale Medical School as an assistant professor in the division of trauma/critical care/emergency surgery." Felix can be reached at [felixlui@gmail.com](mailto:felixlui@gmail.com).



# Alumni Album

## CLASS NOTES

**Jennifer Martinelli Souza '95** WRITES, “My husband and I are happy to announce the October 14, 2005, birth of our first child, Ryan Joseph.” Jennifer can be reached at [jsmarts22@yahoo.com](mailto:jsmarts22@yahoo.com).

**Yuki Young '95** IS A CLINICAL instructor at Mount Sinai School of Medicine in New York City.

**Brenna L. Anderson**, ASSISTANT PROFESSOR of obstetrics and gynecology, has joined the Division of Maternal-Fetal Medicine at Women & Infants Hospital. She completed residency training in obstetrics and gynecology and dual fellowships in maternal-fetal medicine and reproductive infectious diseases and immunology at Magee-Women’s Hospital of the University of Pittsburgh Medical Center. Concurrently, she completed a certificate program and a master of science program in clinical research. Her research interests include the effects of certain sexually trans-

mitted diseases and HIV on preterm birth and pregnancy outcomes.

### 2003

**Roger Han '99** IS A RADIOLOGICAL resident at Tufts-New England Medical Center in Boston, MA.

### 2005

**Jason D. Iannuccilli '00** MARRIED Shawna E. Hassett on June 10, 2006.

**Elizabeth Schoenfeld '01** MARRIED Pranay Parikh '99 MD'03 on August 20, 2006. The bride is a resident in emergency medicine at George Washington University Hospital. The groom is a resident in plastic and reconstructive surgery at Georgetown University Hospital.

### 2006

**Hannah Idiong Awai '00** IS A RESIDENT

at Connecticut Children’s Medical Center in Hartford, CT.

### House Staff 1997

**Michelle Gregory** PRESENTED THE S2 Photo Scanner during a WJAR-TV News Channel 10 segment. The device uses Nobel prize-winning technology to record patient information for nutritional assessment.

### 2004

**Robert Denshaw** HAS JOINED HAWTHORN Medical Associates in Dartmouth, MA, where he treats kidney disorders, including chronic kidney disease, acute kidney failure, and hypertension. He completed a fellowship in nephrology at the University of Pittsburgh Medical Center, where he was chief renal fellow from 2005 to 2006. □

**3**  
**WE  
WANT  
TO HEAR  
FROM  
YOU.**

**2**

## CONTACT!

**1**

Knowing how to get in touch with you is important to us.

So important, in fact, that we’re going to make it interesting.

From now until December 31, all alumni who send us their contact information will be entered into a **special drawing**. Three winners will each receive a Brown Med gift bag packed with **eye-catching merchandise** worth more than \$150, including a Brown Med hat, travel mug, stadium blanket, messenger bag, and more.

So take a moment to fill us in at <http://bms.brown.edu/alumni/> (click on “Fill Us In”) or send your updated contact information, including e-mail address, directly to us at **Med\_Alum@brown.edu**.





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Questions? Call Brown Medical School's Office of Advancement at 401 863-3232 or contact Bethany Solomon directly at 401 863-1635 or [Bethany\\_Solomon@brown.edu](mailto:Bethany_Solomon@brown.edu).

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