VOLUME 7
ISSUE 1
SPRING/SUMMER 2007

DukeMed MAGAZINE

ADVANCES IN RESEARCH, EDUCATION, AND PATIENT CARE AT DUKE

The diabetes epidemic is hitting the country hard—and complicating care in almost every medical specialty. Inside, read how Duke is working to win the

BLOOD SUGAR BATTLES

From Beijing to Broad Street:
Improving health at home and abroad

This April, Duke Medicine was privileged to host a team of leaders from Peking University Health Science Center, one of the most respected health care systems in China. As some of our readers may recall, Duke and Peking University last year signed a letter of intent to work together to improve health care management and cardiovascular medical education, research, and care.

During their recent visit, the Chinese delegation spent 10 days here learning about Duke University Health System, with the goal of gathering ideas for better integrating their own system of eight hospitals and 11 schools.

We are applying our energies and intellectual capital to develop innovative models for delivering care more effectively and efficiently to people across the economic and geographic spectra.

As Peking University executive vice president Ke Yang, MD, stated, "Since the late 1980s, Chinese hospitals have been losing their subsidies from the government, so they are faced with operating in a market-based economy. Duke's experience with establishing a multi-hospital system should provide us with important lessons that we can take back to China."

Duke Medicine and Peking University's mutual goal is to find solutions to the widespread problem of health disparities. While some hospitals in Chinese urban centers are comparable to Western medical centers, good care is scarce and often unaffordable for the 900 million people living in impoverished rural areas. By finding ways to operate more efficiently, Peking University hopes to be able to extend medical services to a greater percentage of the country's growing population. Accordingly, Duke and Peking University Health Science Center will establish a strategic partnership to develop models of integrated academic health systems to address these important global issues.

The problem of health disparities and lack of access to care is hardly unique to China. Even in the United States, which spends more money on health care than any other country in the world, nearly 47 million people have no health insurance. Many of these individuals have difficulty obtaining even basic preventive services—including thousands living right here in Durham, the "City of Medicine."

Duke Medicine has worked to meet the needs of the poor and underserved in Durham and the Carolinas since its founding. In fiscal year 2006, for example, Duke provided charity medical care at a cost of $40.4 million, plus $63.9 million in unreimbursed care to Medicare/Medicaid patients and $7.1 million in in-kind service contributions and direct support payments to Lincoln Community Health Center and Durham County EMS.

Such contributions make a tremendous difference for many in our community. But as a leading academic health system, we can make an even greater impact on health disparities—both locally and globally—by applying our energies and intellectual capital to develop innovative models for delivering care more effectively and efficiently to people across the economic and geographic spectra.

I am particularly excited about one such effort: the new Duke Center for Community Research (DCCR). Part of the Duke Translational Medicine Institute, the DCCR, led by Lloyd Michener, MD, will work closely with local leaders, clinicians, and residents to develop model systems for improving the health status of Durham County. By figuring out better ways to bring advances in scientific and medical knowledge to the people of Durham, the DCCR hopes to better address the needs and concerns of our community while producing measurable improvements in its health within five years. [Editor's note: Read more about the effort on page 52.]

Even more encouragingly, the knowledge we gain here about the best ways to prevent and treat illness on a community-wide basis will benefit people far beyond Durham. Thanks to our Duke Global Health Institute and relationships with other health care providers in China, Singapore, Tanzania, and beyond, we have an unprecedented ability to share the lessons we learn here with others worldwide—and to benefit from their experience and expertise in turn.

For 76 years, Duke Medicine has been committed to improving health care in the Carolinas. As we develop these new initiatives and collaborations at home and abroad, we are well on our way to doing the same on a truly global scale.

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DukeMed MAGAZINE

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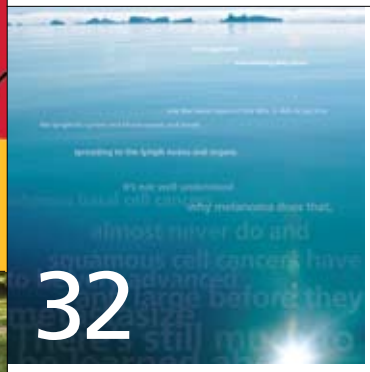
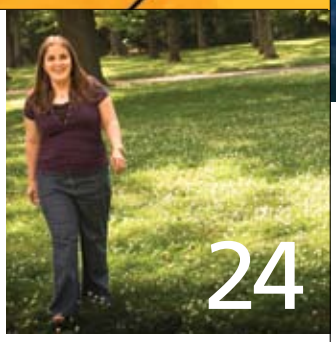
Blood sugar battles

As diabetes cases multiply, Duke caregivers are mobilizing in new ways to keep the disease under control—in the hospital and out.



Beneath the surface

Delving into the mysteries of melanoma—one of the few cancers that remains stubbornly on the rise.



Thinning a generation

Strategies to help children stay healthy in a super-sized world.

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Myozyme: More on a big story

WE WERE DELIGHTED TO RECEIVE DOZENS OF LETTERS FROM readers in response to our last issue—many commenting on the new design of the magazine, and even more on the contents.

One story in particular seemed to strike a chord: "The Making of a Miracle," which chronicled the development of a lifesaving therapy for Pompe disease, a genetic disorder that was previously fatal in newborns. The new treatment, Myozyme, discovered by Y.T. Chen, MD, PhD, and his team at Duke, was approved by the FDA in April 2006.

Reader Jesse Samuels, MD'67, a medical director of Aetna in Connecticut, was especially enthusiastic. He wrote: "The article in this current issue, 'The Making of a Miracle' by Marsha Green and Kathleen Yount, was superb! It was (from what I know) clinically quite correct, beautifully written, had a very important message about the value of medical research, and makes Duke look very good. I will share this article with our nurses who are involved in decisions about [insurance] coverage for these patients.

"It was such an excellent piece of writing that I hope you have thought of submitting it to a lay publication, such as the *New Yorker*, or the Sunday *New York Times Magazine*, so Duke and its researchers can receive wider recognition that is so well deserved."

If you missed the story of Duke researchers' successful search for a treatment for Pompe disease in our Fall/Winter 2006 issue, find it on our Web site: dukemedmag.duke.edu.

We agree that this inspiring story deserves a broad audience—and are happy to report that it is finding one. Pulitzer Prize-winning reporter Geeta Anand wrote an article about two families of Pompe patients treated at Duke that appeared in the December 12, 2006 *Wall Street Journal*; she also authored a book on the topic, *The Cure*, which is available through major booksellers.

As any member of the Pompe team at Duke will tell you, even better than these stories is the reality behind them. To date, Myozyme has provided a new lease on life to more than 700 patients in over 35 countries around the world.

Now *that's* a happy ending.

We'd like to hear from you, too!

Comments, criticisms, suggestions? Write to *DukeMed Magazine* at dukemedmag@mc.duke.edu or Editor, *DukeMed Magazine*, DUMC 3687, Durham, NC 27710.

DukeMed Magazine is proud to have received the 2007 Grand Award for special-interest magazines from the Council for the Advancement and Support of Education District III (CASE III), whose members include academic institutions throughout the Southeast.

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WILL MCINTYRE

Duke Med Scholars

(or, How to Build a Great Faculty When Times Are Tight)

by R. Sanders Williams, MD
Dean, Duke University School of Medicine
Founding Dean, Duke-NUS Graduate Medical School Singapore
Senior Vice Chancellor for Academic Affairs

A faculty appointment at a private medical school like Duke has waggishly been likened more to a hunting license than a job. This description exaggerates a bit, but the truth of the matter is that medical school faculty members are, to a large degree, individual entrepreneurs. Each one, through successful competition for grants or by fee-for-service medical practice, must generate revenues to pay most of their own salaries and to support staff and other costs of their research and academic activities.

IN THE MOST EXTREME circumstances this state of affairs has been termed, rather uncouthly, "eat what you kill"—a strange directive for persons skilled in the healing arts, but apt enough to be an oft-spoken phrase. Tuition dollars contribute to the salaries of faculty active in teaching, but are a minor component of faculty support overall. Endowed chairs are wonderful, but are available only for a very few (Note: we need more!). Further, they usually are awarded only after a senior faculty member has become an established star. For junior faculty we provide a modicum of institutional support as start-up funding while they establish themselves, but within a few years they are expected to be largely self-sufficient.

This economic system is fundamentally the same at all the leading private academic medical centers, and has served us well for many decades. Its Darwinian principles have provided powerful selective pressures to enhance faculty quality. Its drawbacks, however, are being magnified by the recent downturn in federal grant funding and by almost a decade of declining reimbursement to clinicians per unit of work performed. Our faculty feel the squeeze in their personal and professional lives, and there are other dangers that threaten academic medicine more broadly: An overemphasis on individual entrepreneurism in research may discourage collaboration or sharing, and it encourages "safe science," i.e. pursuing work most likely to attract grant funding in the near term to the detriment of more daring research with potential to lead to major breakthroughs. In addition, a sense of uncertainty and instability inherent to such an economy may, in lean times, become too much to bear for some faculty, who may depart academic life for other, more lucrative and (ostensibly) safer and more predictable jobs in private practice or industry. Finally, the system provides little opportunity for faculty to seize the moment—to follow through aggressively on a brilliant idea.

There should be a better way, you will say, and now there is, or at least the beginnings of such, under the umbrella of the School of Medicine's strategic plan: the Duke Med Scholars program. A faculty committee, led by Vice Chancellor Peter Agre, MD, has been formed to evaluate candidates for this new type of award, and this group has codified a process and a set of criteria by which candidates for Duke Med Scholar awards should be judged.

Their charter reads: "The Duke Med Scholars program seeks to honor and support a unique group of faculty members at Duke University School of Medicine who have distinguished themselves through past achievements and who hold promise of still further achievements of particular distinction. The two major goals of this program are to attract exceptional new faculty to Duke and to accelerate progress of current faculty who are judged most likely to generate high-impact work. Scholars will be chosen from basic, translational/clinical, and educational investigators who represent the best of Duke academic medical sciences."

Recipients will be diverse in all respects, but will share a common characteristic—each will be poised to make rapid progress towards a position of true intellectual leadership in their respective fields. Financial support from the award is designed to come at just the time in their career when extra resources can have the most impact, and is generous enough to allow faculty to focus fully on their research—instead of on how they are going to fund it. The program, now in its first year, awarded the inaugural Duke Med Scholar Awards in February to six extraordinarily gifted young investigators. We expect great things of them, and will be calling upon our alumni and supporters to help us to expand this program to reach a larger fraction of our faculty in future years.

Read more about the first class of Scholars on page 48.

Honoring a life's work: saving lives

SOME DISEASES CAN KILL before they are even diagnosed. Among them are the primary immunodeficiency diseases, or PIDs—and these are among the most heartrending, because PIDs often claim the lives of the very, very young.

Pediatric immunologist Rebecca Buckley, MD, has made a career of turning such tragedy into miracle. A longtime Duke faculty member, she has treated and researched PIDs for some 40 years—almost as long as the field of pediatric immunology has been around. Now a designation honoring the work of Buckley and other Duke experts in pediatric immunology will help reinforce their efforts.

The Immune Deficiency Foundation, a national patient organization, has named Duke a Center of Excellence for Primary Immunodeficiency Diseases. Buckley directs the new center, which supports 21 physician-scientists, nurses, researchers, and staff. A grant from Talecris Biotherapeutics will help purchase equipment to aid the center in one of its central missions: diagnosing PIDs with speed and accuracy.

Some PIDs, when caught early, can be successfully treated, and most are very easy to screen for. But they almost never are—at least not until a person becomes dreadfully ill, says Buckley. For example, she says, one of the easiest screenings involves a simple blood count with manual differential to check for a low lymphocyte count, which can signal serious immune disorders such as severe combined immunodeficiency disorder (SCID), or "bubble boy" disease. "When I was an intern and resident, we would do these kinds of tests all the time," says Buckley. "But nowadays, HMOs don't want to pay for that."

"Since 1982 we've performed 158 bone marrow transplants in 'bubble-boy' infants here at Duke, with an overall survival rate of 78 percent." —Rebecca Buckley, MD

In the absence of screening, PID diagnosis can take years—primarily because these diseases are unfamiliar to both patients and health-care providers. Additionally, there aren't many medical centers in the country that specialize in diagnosing PIDs. "Those who are familiar with PIDs are already familiar with Duke's experience in treating them," says Buckley. "But most people aren't aware of either. This new center of excellence will help that; now, when the IDF gets calls from new patients, they can refer them here."

The grant from Talecris will buy Duke's center a new real-time PCR (polymerase chain reaction) machine. "This equipment gives us what we need to determine, in conditions where T-cell function is abnormal, whether it's due to something external or to a genetic defect," says Buckley.

Such measurements are useful in diagnostics as well as in research. Buckley is currently following children who have received stem-cell transplants to treat SCID, a condition that is uniformly fatal in infancy unless diagnosed and treated properly. Buckley pioneered the lifesaving transplant in 1982; her oldest patient is now 25. "When we transplant SCID infants in the first 3.5 months of life, our survival rate is 96 percent," she says.

"When I first came into this field, only one [PID] was known," adds Buckley. "Before 1952 these illnesses were attributed to some bad germ in the environment. And there's just been an explosion of information since then—more than 150 PIDs have been identified so far.

"I used to watch these babies die all the time. Since 1982 we've performed 158 bone marrow transplants in 'bubble-boy' infants here at Duke, and we have an overall survival rate of 78 percent. It makes me enormously happy for these children and their families."

Did You Know:

Duke earned its designation of excellence because of its longstanding strengths in treating primary immunodeficiency diseases, including:

- The most faculty in the United States with expertise in primary immunodeficiency
- The development of sophisticated diagnostic testing utilized nationwide
- The largest center in the world that performs non-ablated T-cell-depleted haploidentical bone marrow transplants in SCID infants
- Extensive experience in immunoglobin treatment for antibody deficiency
- The world's only center performing thymic transplants for infants with complete DiGeorge syndrome (led by Louise Markert, MD). A recent Duke study showed that 75 percent of infants who received the transplant were alive after one year.

Duke in Singapore

An update on the Duke-NUS Graduate Medical School

2007 IS SHAPING UP TO BE a banner year for the Duke-National University of Singapore (NUS) Graduate Medical School Singapore (GMS).

In January, the Estate of Tan Sri Khoo Teck Puat announced a gift of S$80 million to the GMS to grow the school's biomedical research initiatives. The gift, the largest single donation granted by the Estate to date, will be matched by the Singapore government, bringing the total sum to S$160 million (about $104 million US dollars).

The GMS also announced that graduates of the four-year GMS program will be awarded a joint medical degree from Duke University and the NUS. This follows the recent decision by Duke's Board of Trustees to approve the granting of the joint degree.

The Estate's generous gift will enable the GMS to substantially accelerate and strengthen its planned research programs, which are focused on medical and health care problems of significance to Singapore and Asia. The gift will support groundbreaking research across GMS's four Signature Research Programs in infectious diseases, cancer and stem cell biology, neurobehavioral disorders, and cardiovascular and metabolic disorders.

In recognition of the Estate's generosity, the GMS will name its new signature building the "Khoo Teck Puat Building." To be completed in 2009, the building will house state-of-the-art research, educational, and administrative facilities.

The GMS, established in April 2005, will enroll its first class of 25 students in August 2007; subsequent classes will comprise 50 students each year.

Richard Frothingham, MD

The best-dressed docs at Duke

Forget the respect commanded by a white coat—this ensemble takes the cake. Personnel who work in the Global Health Research Building must undergo a federal background check and be trained in handling dangerous pathogens. Then, when they get to work in the morning, those who work with pathogens don special attire, including seamless gowns, gloves, foot covers, and respirators. Their work stations are biological cabinets whose air is individually filtered. The rooms are sealed by an epoxy floor and epoxy paint on the walls. Before heading home, personnel are able to "freshen up" in showers designed to remove potential contaminants. All this in a security-zoned complex, so no wandering to the neighbor's yard without authorized access.

Defense against man and mosquito

DUKE HAS BUILT a new stronghold of defense against an array of biologic public health threats, from anthrax to West Nile Virus. The nation's first Regional Biocontainment Laboratory, funded by the National Institutes of Health, has opened here to develop the next generation of vaccines, treatments, and diagnostics for protecting citizens against emerging threats to public health.

"Because we live in a global society, infections that arise anywhere in the world can quickly become relevant to us," says Richard Frothingham, MD, director of the facility, which will be available to researchers at Duke and other universities throughout the Southeast. Twelve similar facilities nationwide will follow close on the heels of Duke's lab, which was named the Global Health Research Building.

An "open fortress" may be the best way to describe the $22.4-million building. The research conducted there is not classified, and open collaboration across campus and with other institutions is encouraged, yet the building has been constructed under the most stringent interpretation of federal guidelines for security and safety. Surrounded by a fence, monitored by security guards, and supported by pillars capable of withstanding both hurricanes and tornadoes, the building houses research on pox viruses, plague, influenza, and tuberculosis. These microbes are handled at Biosafety Levels 2 and 3, the levels the building was designed to accommodate. No research will be conducted on Biosafety Level 4 microbes, such as smallpox or Ebola virus.

Stubbing out tobacco

LONG GONE ARE THE DAYS when clinic waiting rooms held ashtrays and advertisements had the family physician endorsing Luckies, Chesterfields, or Camels. Yet while Duke University Medical Center has had smoke-free facilities since 1989, the last gasps of a smoking section are just now being extinguished for good. As of July 4, 2007, all Duke Medicine campuses will be completely tobacco-free, with no smoking or tobacco use permitted indoors or out—including in previously designated outdoor smoking areas. Duke joins other Triangle-area hospitals in making the July 4 transition, designed to promote a healthy environment for patients, visitors, and employees.

For more information, visit dukemedicine.org/tobaccofree.

A Carolina beauty: Duke's new ED opens

IN APRIL DUKE'S new Emergency Department opened its doors for business. And though few people ever look forward to visiting an emergency room, Duke's new facility offers the best in technology as well as some soft touches to bring life into this life-saving sanctuary. "This is still only phase three of our complete plan," says Kathy Finch, ED construction coordinator. "But opening the new building allowed us to move most of our patient care out of the old ED so that we can now renovate that as well. By December 2007, we hope to have all of the work done."

When the renovations are complete, the new ED will be home to:

- three 12-bed, self-sufficient adult-care units, equipped with their own nursing stations, supply areas, and resuscitation bays
- a separate, 18-bed pediatric area, including two critical-care rooms and isolation rooms
- computers in every patient room
- a 7,000-square-foot ambulance bay with an entry located well away from the front door
- two fully equipped x-ray rooms, a dedicated CT scanner, and a fluoroscopy room
- decontamination showers, as well as decontamination capability for the entire ED
- secured doorways, a security checkpoint, and an office for police liaison.

The high-tech units are decorated throughout with scenic, soothing images taken from North Carolina's varied landscape.

Perhaps the best thing about the new ED is its size. The previous ED, built in 1981, was designed for 40,000 patients per year—Duke currently sees around 60,000.

"Once all of our renovations are complete," says Finch, "we will have doubled our space and be able to handle 90,000 patients per year."

Natural touch: The front entrance to the ED features a 20-foot collage of North Carolina's best and most beautiful scenery, from the mountains to the Piedmont to the coast.

Taking on care disparities

STUDIES HAVE SHOWN that African Americans and Latinos suffer persisting inequalities in cardiac care. And, as Duke University Hospital CEO William J. Fulkerson, MD, says, it is our obligation to right such injustices. "Our responsibility is not only to deliver high-quality care, but also to deliver care equitably. That's our job."

"Our responsibility is not only to deliver high-quality care, but also to deliver care equitably. That's our job." William J. Fulkerson, MD

Fulkerson is the executive sponsor for Duke's participation in a national effort to reduce health-care disparities. The "Expecting Success" program, sponsored by the Robert Wood Johnson Foundation, is a 29-month collaboration among 10 medical centers across the nation. These institutions are examining current practices, experimenting with improvements, and sharing ideas, programs, and findings to identify "best practices" to equalize care for all patients.

At Duke, the process begins with information, so staff have now begun collecting race and ethnicity information from all patients who register in the hospital. "This process will help greatly to describe populations and understand how patients are served," says cardiologist Eric Velazquez, MD, the program director for Expecting Success. "This will help us develop a strategy to minimize disparities."

But race and ethnicity are also sensitive and personal information, and in a hospital that sees 4,000 patients every day, two extra info items per patient is a tremendous increase in data. So the hospital underwent a massive preparatory campaign, including retooling of IT infrastructure, staff training for cultural competency, and information for visitors and patients.

Velazquez says the process has started off well, and that it will have big implications for improvements in patient care. "We're raising awareness of disparities at both the patient and the provider levels," he says, "in addition to leveraging the experiences and knowledge of nine other major medical centers across the country."

"Bundle up" to prevent bloodstream infections

TO EVERY HOSPITAL, there is an ICU, and to every ICU, there is a CVC (central venous catheter)—several, actually, as 48 percent of patients in intensive care units require these catheterizations. Unfortunately, CVCs can also cause dangerous and costly bloodstream infections. Nationally, between 14,000 and 28,000 deaths every year are attributable to catheter-related bloodstream infections. "And a single case of infection can cost from $25,000 to $65,000," says Duke anesthesiologist Nancy Knudsen, MD.

Knudsen led Duke's effort for the national "100,000 Lives" campaign conducted last year to reduce preventable hospital deaths. Part of Knudsen's strategy was to make CVC training—long available to house staff as an online course—mandatory.

The training course, created by Keith Kaye, MD, and John Grant, MD, is available online to all Duke staff and medical students. It's also provided for training in all 35 Southeastern hospitals that are members of the Duke Infection Control Outreach Network (DICON), and other hospitals nationwide that DICON serves. "Since January 2006, 1,300 people have taken the course," says Paul Thacker, administrative director of DICON.

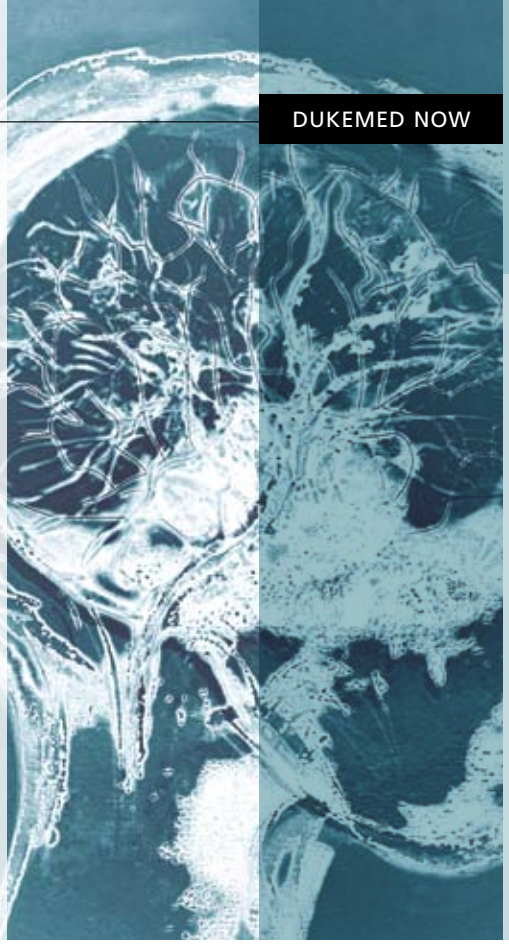
The course, fully updated last summer, teaches physicians what's called the CVC bundle: a set of five standard concepts that, when completed as a unit, improve clinical outcomes in patients with CVCs. The concept means that, instead of completing five tasks as part of inserting a CVC, the five components are "bundled" in the protocol—and the physician's mind—as one intervention. The bundle includes hand hygiene, maximal sterile barrier precautions, chlorhexidine skin antisepsis, optimal catheter site selection (subclavian preferred), and daily monitoring of line necessity with prompt removal of an unnecessary line. Duke's online training includes video demonstrations, slides, and pre- and post-tests.

ICUs that implement CVC bundling well are reporting near elimination of catheter-related bloodstream infections.

The 100,000 Lives campaign was spearheaded by the Institute for Healthcare Improvement (IHI). In 18 months, 3,100 participating hospitals saved some 122,000 lives by improving hospital standards and bringing attention to potential patient harms. Now the IHI has launched a "5 Million Lives" campaign, which will run through December 2008.

To learn more about Duke Infection Control Outreach Network, visit dicon.mc.duke.edu.

To learn more about the 5 Million Lives campaign, visit the Institute for Healthcare Improvement site at www.ihi.org.



Exploring the neural frontier

ALCOHOLISM, CARDIOVASCULAR DISEASE, autism, Alzheimer's, violence—these ills of the world all involve a complex and poorly understood interplay of neurobiology, genes, behavior, and emotion. Duke is taking a new approach to penetrating the mysteries of the mind through its Institute for Brain, Mind, Genes, and Behavior.

Launched in December 2006, the institute will promote innovative projects that explore questions of thought, emotion, and behavior. The interim co-directors—Ranga Krishnan, MD, Dale Purves, MD, and Timothy Strauman, PhD—say it also significantly expands educational opportunities at Duke in neuroscience. The institute will fund at least two multiyear projects this year, the findings from which could help provide scientific rationales for government and social policies in areas as diverse as education, law, ethics, and religion.

"The emergence of neuroscience and its interface with medicine, behavioral science, and policy is likely to add important new tools for understanding why people behave as they do," says Strauman. "How such insights ultimately will be used will be limited only by society's collective imagination."

A healthy new start for homeless families

THE PHRASE "Think Globally, Act Locally," is surely trademarked by an environmental group by now. But it would be a good slogan for the Duke School of Nursing's new Office of Global and Community Initiatives (OGACHI), directed by Dorothy Powell, EdD, RN. Though the office develops nursing programs in countries around the globe, one of their first projects was right here in Durham—and it was also something of an accidental blessing.

Powell chanced to meet Graham Fitzsimons, the board chair of Durham's Genesis Home, a transitional shelter for homeless families. In this introduction the seeds were planted for the "Raising Health, Raising Hope" program, in which eight students in Duke's accelerated bachelor's in nursing program teach monthly health courses to families living at Genesis Home. The program was so successful in its initial trial that leaders decided to make it a permanent resource for the Genesis Home—and for nursing students, who gain valuable experience in providing health education.

The students shape the courses based on requests from the Genesis Home residents themselves, most of whom are single mothers. The initial workshops covered issues such as dental hygiene, healthy cooking and nutrition, exercise and wellness, and women's health, and offered both information and practical tips. In the exercise course, for example, the nursing students used sand-filled water bottles to teach the mothers how to get a quick workout at home.

Powell says that homelessness is sure to become a hallmark theme for OGACHI, which was established in January 2006. "Many homeless people feel hopeless and have a poor self-concept," she says. "These courses have raised their awareness of health issues," which often get little attention from women struggling to find safe housing and food for their families.

Nursing student Amy Runk teaches kids at Genesis Home about healthy dental habits.

For more information about Genesis Home, call 919-683-5878. To learn more about the local, state, and international programs in OGACHI, call 919-684-9301.

Pressing question:

What should doctors do to protect patients with drug-eluting stents?

If drug-eluting stents can sometimes lead to formation of lethal blood clots, as recent much-publicized studies have shown, just how long should stent patients stay on the anti-clotting medication clopidogrel (Plavix)? The new studies have physicians speculating that an update may be in order for the current recommendation, which is 12 months of post-stenting aspirin and clopidogrel therapy. Duke cardiologist David F. Kong, MD, co-authored one of the recent stent studies (published in the December 5, 2006 *JAMA*), so we asked him for some input. He says that this issue, like most others in medicine, is more about judgment than juggling statistics.

David F. Kong, MD

Given the revelations about drug-eluting stents, should physicians prepare these patients to remain on clopidogrel indefinitely? We choose the word *indefinitely*, as opposed to *forever*, for a reason—because we don't yet know what the endpoint might be. We're in a situation where our technology has leapt beyond our understanding of the biology of the systems the technology is affecting. For now, we recommend most patients on clopidogrel continue with it until we learn more.

There is difference of opinion on how to advise patients who took clopidogrel but have since stopped. What's your take? In my opinion, if that patient has been off the drug for a year and is doing well, then his or her risk for an event is comparatively low. If an event were likely to happen, it is most likely that it would have occurred within that year.

However, it's important to emphasize that each patient should discuss this decision with his or her physician, because there might be other reasons for that patient to be on this kind of drug.

How do you apply the results of your study to each patient? In general, the probability that a clotting event will happen isn't determined in a vacuum. So the statistic that we have—eight clotting events per thousand—isn't the ultimate measure of one individual's risk. Some patients may be at higher risk than that, others at lower risk.

If you are in an auto accident, your chance of dying in that accident is six per thousand. Now, we don't stop driving cars based on this risk, but at the same time, the risk is big enough that we want to do what we can to minimize those odds, such as including airbags and seatbelts in cars. It's the same principle.

Do side effects of clopidogrel factor in your decision? The principal risk of this drug is bleeding events. Few of these are fatal, but there's a 1 percent chance per year, if you're taking clopidogrel and aspirin, that you'll have a bleeding event serious enough to see your doctor about. So that's a higher risk than clotting, though it's for a less serious event.

Another thing to consider is that the patients who are on clopidogrel now are a self-selecting population; we know they tolerate it well or they wouldn't be taking it.

What about cost? People have debated that a lot. Plavix costs between $3.50 and $4.00 per day. But again, this is a factor that is weighed in terms of the patient—for some that's a greater burden than for others. And, if you think about it on a grander scale, you can say that while this drug costs $1.5 to $2 billion a year worldwide, we spend about $30 billion per year on potato chips.

Our job as physicians is to help patients make informed decisions about treatment. In every situation we're implicitly making those judgments and prognostications, to help a patient make the choice that's best for him or her. That's what makes medicine an art.

Drug-eluting stents: the end of an era?

A large study published in March in the *New England Journal of Medicine* confirmed the mounting results of smaller studies, including those conducted at Duke, showing that drug-eluting stents have a limited ability to prevent future cardiac events. Robert M. Califf, MD, who co-authored one of the Duke stent studies, says that this crop of research may cause some shift away from drug-eluting stents; cardiologists may recommend more of their patients for bare-metal stents, bypass surgery, or secondary prevention such as lifestyle modification and drug therapy.

But he emphasizes that drug-eluting stents will not lose their place in the cardiology tool-chest. "They are still a very good thing to have for patients with unstable symptoms," he says. "These studies have been on patients whose symptoms were stable." Califf also says that it's important to remember that medical technology is always evolving. "In a reasonable period of time," he believes, "this issue will be obsolete."

Not your mother's hysterectomy

MINIMALLY INVASIVE GYNECOLOGY means more than just laparoscopic surgery. For those at the Duke Center for Minimally Invasive Gynecologic Surgery, it entails a whole philosophy of care.

"It means providing care for women that focuses on making a positive impact without adversely affecting quality of life," explains Craig J. Sobolewski, MD, the center's co-director and chief of Duke's Division of Gynecologic Specialties. "Sometimes that means prescribing innovative medical therapy. Sometimes it means offering procedures that were traditionally done in the operating room in a clinic or office setting."

Such procedures include hysteroscopy, viewing the inside of the uterus through a thin, telescopic tube to evaluate and possibly treat bleeding via endometrial ablation, which offers an alternative to hysterectomy. When necessary, hysterectomy itself can often be performed "approaching through tiny abdominal incisions utilizing a lighted telescope [laparoscope] instead of making a standard open abdominal incision," says Sobolewski. "This is not your mother's hysterectomy."

The center, which opened in June 2006, has also recently begun offering Essure, a new permanent sterilization procedure not yet widely available in most offices. Essure involves inserting spring-like coils through the vagina, cervix, and uterus into the fallopian tubes to help the body form a barrier and prevent sperm from reaching the egg. The procedure does not require incisions or general anesthesia. "For years, men have been able to have a vasectomy performed in a doctor's office," says Sobolewski. "Essure is much safer than a traditional 'tubal' done through the belly button, allowing us to offer women an office-based procedure also."

Sobolewski is joined by co-director Jeffrey P. Wilkinson, MD, a urogynecologist specializing in the treatment of urinary incontinence and pelvic organ prolapse, and colleagues Stanley J. Filip, MD, and nurse practitioner Alice P. Cooper. All are faculty in the School of Medicine. "We're providing women's health care in the community, but we're still academicians," says Cooper. "We're thinking about the latest research and the latest outcomes-based care, and we're providing it in a friendly, easy-to-use place."

(left to right) Alice P. Cooper, RNC, OGNP, Stanley J. Filip, MD, Craig J. Sobolewski, MD, and Jeffrey P. Wilkinson, MD

Contact the Duke Center for Minimally Invasive Gynecologic Surgery at 919-684-2471.

The trials of Duke Medicine

FROM NEW CHEMOTHERAPY PROTOCOLS to a potential treatment for toenail fungus, Duke operates literally hundreds of clinical trials testing novel approaches to patient care. Referring physicians and interested individuals alike can learn about many trials actively recruiting research subjects online at DukeHealth.org. Just click on the "Clinical Trials" button to access a sortable list of some of our current trials as well as links to additional databases.

Endoscopic lung cancer diagnosis

DUKE GASTROENTEROLOGISTS say they can help in the diagnosis of lung cancer. A meta-analysis of 18 small clinical trials—at Duke and other sites—shows that endoscopic ultrasound with fine-needle aspiration is safe and effective for diagnosing and staging possible cancerous masses in the lung.

Successful treatment of lung cancers depends on accurately typing tumors and identifying whether tumor cells have spread to adjacent tissues or lymph nodes. The clinical trials that were analyzed evaluated endoscopic ultrasound's accuracy in detecting the spread of non-small cell lung cancer in 1,201 patients. Non-small cell lung cancer, which represents about 80 percent of all lung cancers, is a fast-growing, often fatal form of the disease.

If the procedure were universally adopted, almost one-third of lung cancer patients could be spared more invasive staging procedures, say the researchers, who believe that the ultrasound procedure should be used routinely to evaluate possible malignant masses. The study appeared this February in *Chest*.

The tales garbage tells

CARDIOLOGIST SVATI SHAH, MD, says it's a bit like going through someone's garbage can to learn more about him. She and a team of Duke researchers have sorted through the bloodstream's metabolic "trash" to identify new markers for measuring cardiovascular health. These markers, called metabolites, may prove useful as early warning signals for impending coronary artery disease.

The analysis is among the first to use metabolomics—the systematic study of the unique chemical traces that specific cellular processes leave behind—to better understand underlying biological pathways in families with coronary artery disease.

Researchers led by Christopher Newgard, PhD, of Duke's Sarah W. Stedman Nutrition and Metabolism Center, studied these chemical traces in blood samples of people whose extended family members developed coronary artery disease at an early age. The team then identified which metabolic profiles signify increased susceptibility to heart disease and showed that these profiles were heritable in families. "With this advance notice of genetic predisposition to heart disease, we could start strategies, such as drugs or lifestyle changes, to stop or slow down the disease process," says Shah, who presented the findings at the 2006 American Heart Association scientific sessions.

A new clue to heart disease

RESEARCHERS SIFTING through the genomes of siblings in families with high incidence of heart disease may have unearthed a genetic gold nugget. On chromosome 3 they identified a new gene, called kalirin, that may indicate a high risk for the disease. The gene implicates a biological mechanism never before linked to cardiovascular disease—and its discovery may lead to new clinical tools to treat or even prevent heart disease. The Duke study was published in the April 2007 *American Journal of Human Genetics*.

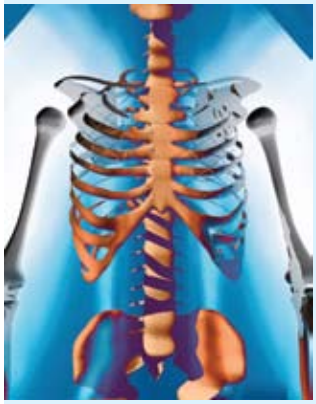
Give Fosamax five years, it gives you 10:

What a recent study may mean for osteoporosis patients

The bisphosphonate drug alendronate (Fosamax) is doubling its returns to women with osteoporosis, according to a recent national study. Patients who take the drug for five years have nearly the same protection from bone fractures as patients who take it for 10 years.

We asked Duke geriatrician Cathleen Colón-Emeric, MD, what physicians should take away from this study. Colón-Emeric, who wrote the editorial that accompanied the study in the December 27, 2006 *Journal of the American Medical Association*, says patients who have done well on alendronate can safely consider a "holiday" from the drug. This option would apply only to those who have not suffered a fracture and have had a significant improvement in their bone density.

Should osteoporosis patients on other bisphosphonates consider switching to alendronate? The study was a comparison of alendronate versus a placebo. So it doesn't make any comparisons in the effectiveness between alendronate and other medications.



Should all patients who are now taking alendronate—who don't develop fractures or drops in bone density—expect to be able to quit after five years? Patients who have a high risk of spine fractures, either because of extremely low bone density or previous vertebral fractures, would want to consider their risks carefully before they stopped taking the medication. This is because the 10-year course was significantly better in reducing new vertebral fractures. But for those who have had a good response to the drug and have not had previous fractures, a holiday would be a reasonable choice.

If a patient has opted not to take a bisphosphonate, should she reconsider? It depends on why she chose not to take the drug. Those who are at high risk of serious side effects such as uveitis, esophageal ruptures, or osteonecrosis of the jaw when taking this class of medications should not be offered the drug.

However, lots of patients and prescribers choose not to take this drug because of concern over acid reflux. If that is the case, they may find it worth reconsidering.

After five years off of alendronate, is it likely that most patients would need to go back on medication? We don't currently know the effect of restarting alendronate or a similar medication after a drug holiday. It will be increasingly important to carefully monitor patients' bone density during therapy and during the drug holiday. If there were a drop in bone density, the patient would need to consider going back on the drug, or switching to another class of medications.

Growing new cartilage:

Like biomedical basket weaving

Nestling ground: Most machines that produce bioengineered tissue fabrics weave one set of fibers that are oriented perpendicularly to another set of fibers. However, the machine that Duke's Franklin Moutos (above right, with Farshid Guilak) developed adds a third set of fibers, which creates a three-dimensional product. Also, since the scaffold is a woven material, there are tiny spaces where cartilage cells can nestle and grow.

A GRADUATE STUDENT in Duke's Orthopedic Bioengineering Laboratory has built a type of weaving machine that can make three-dimensional fabric scaffolds to improve repair of damaged joints. The student, Franklin Moutos, says the technology will allow physicians will to use their patients' own stem cells to repair hips, shoulders, and ultimately any type of cartilage damage.

In laboratory tests, the synthetic fabric scaffold was shown to have the same mechanical properties as native cartilage. In the near future, surgeons will be able to impregnate the custom-designed scaffolds with cartilage-forming stem cells and chemicals that stimulate their growth and then implant them into patients during a single procedure. "Once implanted, the cartilage cells will grow throughout the scaffold, and over time the scaffold will slowly dissolve, leaving the new cartilage tissue," says Moutos.

Biomedical engineer Farshid Guilak, PhD, senior investigator in a study of the scaffold, says that current treatments for joint cartilage damage are fairly limited. The only bioengineering approach available requires a weeks-long process of growing new cartilage from a patient's cells, and, unlike the scaffold, can only be used for small repairs. "This scaffold will give surgeons the opportunity to treat their patients immediately—patients won't have to wait for months with a painful joint," he says. "And one of the beauties of the system is that since the cells are from the same patients, there are no worries of adverse immune responses or disease transmission."

The study appeared in the February 2007 *Nature Materials*.

Meds for kids: a Congressional battle reheats

UNEXPECTED, INEFFECTIVE, even dangerous outcomes: The problem of prescribing adult drugs to kids goes way beyond dosage, according to a Duke study published in the February 7 *JAMA*. Its authors hope the study will help sway Congress to renew a pediatric drug testing law that expires this year.

Duke pediatricians Jennifer Li, MD, and Daniel Benjamin, MD, analyzed financial and medical data on 59 drugs that were tested in children under the "pediatric exclusivity provision" of the Best Pharmaceuticals for Children Act, which took effect in 1997. The provision encourages companies to run separate pediatric testing of their drugs by allowing a six-month patent extension to drugs that undergo the extra study.

A full third of the drugs tested under that policy were found to work differently in children than in adults. In some cases the drugs were more dangerous for kids, and in other cases they had no effect. Researchers say this finding is unsurprising, since children absorb and metabolize drugs differently than adults.

Critics of the current policy believe that drug manufacturers earn far more in patent profits during the six-month extension than they spend on the tests. They also say that Medicare ultimately foots the bill, as it must pay for name-brand drugs instead of generic during that time.

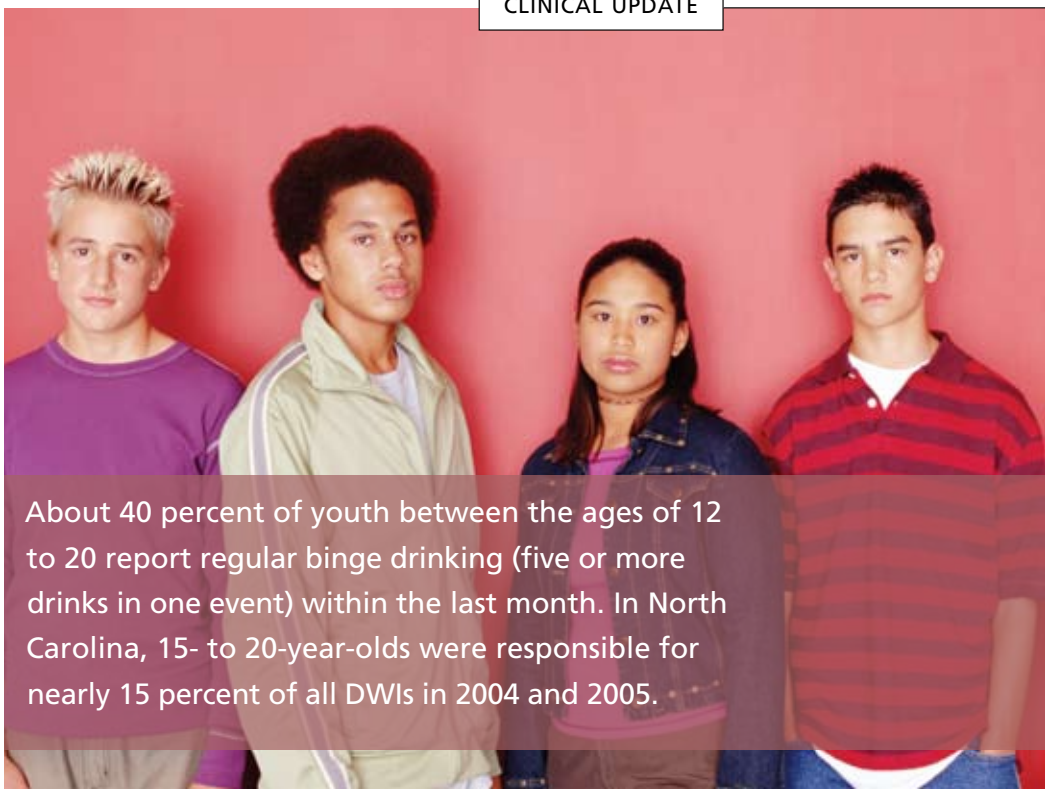
The Duke study found that most drugs in the program made an additional few weeks' worth of sales profits—according to the researchers, a modest return on the vital drug studies in children, which have led to more than 122 labeling changes. The study also showed that most drugs awarded the extension are not among the 200 top-selling drugs.

Benjamin says critics will push to eliminate the program or reduce the patent extension period to three months. "Either step could limit the benefits to children," he says, by cutting the incentive to the drug companies who will "likely cut the number of studies conducted."

At press time a bill to renew the law had passed the Senate and was to go before the House later this summer.

Physicians call 1-800-MED-DUKE (633-3853), patients and consumers call 1-888-ASK-DUKE (275-3853)

Teenage wasteland



About 40 percent of youth between the ages of 12 to 20 report regular binge drinking (five or more drinks in one event) within the last month. In North Carolina, 15- to 20-year-olds were responsible for nearly 15 percent of all DWIs in 2004 and 2005.

IT'S EASY TO THINK that urban adolescents have the highest risk for dangerous behaviors. But when it comes to alcohol abuse, rural teens rise to the top. Four percent of rural teens ages 12 and 13 are regular drinkers, compared with 1.5 percent of their urban counterparts. "For the 14- to 15-year olds, it goes up to 12 percent," says Duke psychiatrist Ashwin Patkar, MD, who, along with principal investigator Robert Hubbard, PhD, is leading a new effort to address underage drinking in these communities.

Duke is one of four sites in the country to receive a PARTNER (Prevention Approaches to Underage Alcohol Use) grant from the National Institute on Alcohol Abuse and Alcoholism. The three-year, $1.6-million grant will fund Duke to work with communities in Durham, Franklin, Granville, Halifax, Person, Vance, and Warren counties to create prevention and treatment interventions for underage drinking designed specifically for these underserved areas, which are home to about 45,000 teens.

Patkar explains that the barriers to prevention and care in rural communities can be profound. Widespread poverty means that many are uninsured, and many others have inadequate insurance for alcohol abuse treatment. Even for those who can afford it, the treatment services available are much more limited (and access is more difficult) than in urban areas. Also, he notes, drinking is a part of the cultural fabric of many rural areas, and stigma in these tight-knit communities precludes the privacy and anonymity that some families need to feel comfortable seeking help for substance abuse.

Duke's PARTNER program will begin by building upon relationships with Duke-affiliated primary-care clinics in these counties to find the best ways to screen for alcohol use as part of standard clinical care.

PARTNER will also establish a referral system with churches, schools, police, and the social services system, so that adolescents who are identified in incidents involving alcohol can be recommended for treatment. "It's really an exciting opportunity to build a stronger relationship between Duke and these communities," says Patkar. "We want to get these kids the help they need now, and find out what will help them best, instead of trying to address even worse problems 20 years down the road."

Nature's call—and answer

A COMMON HERBAL EXTRACT available in health food stores can greatly reduce urinary tract infections and could potentially enhance the ability of antibiotics to kill the bacteria that cause 90 percent of bladder infections.

Duke researchers found that *E. coli* hides in cells lining the bladder, where it cannot be reached by antibiotics. But they also found that forskolin, an extract from the Indian coleus plant, flushes out hiding colonies of bacteria.

"This type of treatment strategy may prove beneficial for patients with recurrent urinary tract infections," says Duke microbiologist and lead researcher Soman Abraham, PhD. "Ideally, use of this herb would expel the bacteria, where it would then be hit with antibiotics. With the reservoir of hiding bacteria cleared out, the infection should not recur."

Abraham says that a new and effective approach for treating urinary tract infections is needed because constant antibiotic use has many drawbacks, including high expense, possible liver and kidney damage, and the potential for creating strains of antibiotic-resistant bacteria.

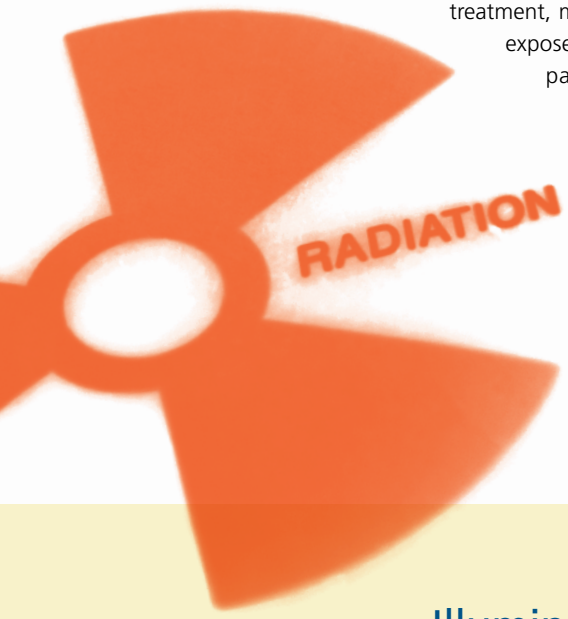
The results were published April 8 in the online *Nature Medicine*.

The herb forskolin can fend off urinary tract infections.

Blood test for a better aftermath

A NUCLEAR OR RADIOLOGICAL catastrophe could expose thousands of people to radiation. The scenario is bad enough on its own—but compounding matters is the fact that, until now, there has been no way of quickly determining how much of the deadly substance has seeped inside an individual's body.

"If a terrorist attack involving radioactive material were to occur, hospitals might be overrun with people seeking treatment, many of whom have actually been exposed and many of whom are simply panicked," says John Chute, MD, of Duke's Adult Bone Marrow and Stem Cell Transplant Program. "We have to be able to efficiently screen a large number of people for radiation exposure in order to respond effectively to a mass casualty event."



There appears to be a critical window of 48 to 72 hours for administering treatments aimed at halting the devastating effects of radiation, investigators say. But existing tests for measuring radiation exposure take several days and are not practical for testing large numbers of patients at once.

Now, Duke scientists have developed a blood test to rapidly detect levels of radiation exposure so that potentially lifesaving treatments could be administered to the people who need them most. The new test scans thousands of genes from a blood sample to identify distinct genomic "signatures" reflecting varying radiation doses. Patients can then be handled according to whether they received no exposure to radiation, intermediate exposure that may respond to medical therapies, or an inevitably lethal dose.

Investigators are currently working to refine the test, and say that the identification of genes that play a role in radiation response could also lead to development of new anti-radiation treatments. Study findings appear in the April 3, 2007, *Public Library of Science (PLoS) Medicine*.

Illuminating altruism

ALTRUISM IS A MATTER of perception, according to a new Duke study. Researchers in the Brain Imaging and Analysis Center explored the brain's activity while subjects played a video game to earn money for themselves or for a charity, and they say their findings may help improve understanding of disorders such as autism, antisocial behavior, and others that are characterized by deficits in interpersonal interactions.

Led by Dharol Tankersley, a graduate student in the lab of neuroscientist Scott A. Huettel, PhD, researchers scanned the brains of 45 people while they either played a computer game or watched the computer play the game on its own. In both cases, success in the game earned money either for the player or for a charity of the participant's choice. The participants also answered questions about how often they engaged in different kinds of helping behaviors, so that the team could characterize each person's altruistic tendencies.

MRI scans showed that the posterior superior temporal sulcus—a region of the brain that works to interpret social relationships—was activated to a greater degree when people watched the computer play than when they played themselves. The level of activity in this area was strongly related to a person's reported tendency toward altruistic behavior. The researchers, who now plan to study the development of this brain region, say these results suggest that altruistic behavior may originate from people's abilities to perceive others' actions as meaningful. Their study appeared in the February 2007 *Nature Neuroscience*.

Hammering home the importance of nail gun safety

ACCORDING TO NEW STATISTICS that would make Bob Vila cringe, the number of weekend carpenters treated each year for nail gun injuries in U.S. emergency rooms more than tripled between 1991 and 2005, increasing to about 14,800 per year, according to a new analysis by researchers at Duke and the National Institute for Occupational Safety and Health.

"These kinds of injuries are often seen as bizarre accidents, but they actually occur fairly frequently and we know quite a bit about factors that contribute to them," says author Hester Lipscomb, PhD, an associate professor of occupational and environmental medicine at Duke. She has long studied nail gun injuries among construction workers, but says this is the first such analysis of injuries among consumers.

Nail guns typically use compressed air to drive nails into wood. Researchers say that many injuries caused by nail guns could be prevented by using tools that fire only when the nose piece is depressed before the trigger is pulled. This "sequential" trigger mechanism is designed to prevent rapid, unintentional firing, but it has not been used as much as tools that allow the user to rapidly "bounce fire" nails.

Lipscomb believes the use of nail guns with sequential-trip triggers will "go a long way toward reducing injuries among consumers and professional carpenters." Kits are available to convert many nail gun triggers to the safer type.

Findings appear in the April 13, 2007, *Morbidity and Mortality Weekly Report*.

Cholesterol: from scourge to supplement?

SO MUCH ENERGY goes into lowering cholesterol levels in adults that it's easy to overlook how important the much-maligned lipid is. Pregnant women with very low levels of cholesterol are actually at risk of giving birth to babies with developmental problems. This is because cholesterol is essential to the proper development of fetuses. It works to regulate a crucial pathway that governs the pattern of tissue development.

This same pathway is vulnerable to the effects of alcohol. According to a new Duke study, even as little as a 12-ounce beer can interfere with this process by blocking the activity of cholesterol. How much interference—and which tissues are affected—depends on at what point in pregnancy the alcohol is consumed.

But the news from these researchers, led by Yin-Xiong Li, MD, PhD, isn't all bad. They found that they could restore normal development in zebrafish embryos that were exposed to alcohol by giving supplemental cholesterol.

"This new insight into the molecular basis of fetal alcohol syndrome could have far-reaching implications," says Li. "It suggests new prenatal care tactics that might prevent the developmental defects caused by alcohol consumed during pregnancy." The team published its findings in the March 2007 *Laboratory Investigation*.

Success stops a cancer trial

A LARGE CLINICAL TRIAL has been halted early because patients taking a new anticancer drug did so much better than patients who did not.

The National Cancer Institute halted the trial in April 2007 so all eligible patients could start taking imatinib (trade name Gleevec) before the planned release of the trial's findings in June.

The multicenter trial, coordinated by the American College of Surgeons Oncology Group (ACOSOG) at the Duke Clinical Research Institute and the Mayo Cancer Center, involved over 600 patients with gastrointestinal stromal tumor. This form of cancer, which develops in muscle tissue and blood vessels within the stomach or small intestine, is estimated to occur in more than 5,000 Americans each year.

The researchers found that 97 percent of the patients who received imatinib were cancer-free one year after surgery to remove their tumor. In comparison, 83 percent of patients who did not take the drug were cancer-free after surgery.

"This is a whole new kind of cancer treatment…that represents the future of oncology," says Duke surgeon and ACOSOG co-chair David Ota, MD. "Instead of one-size-fits-all drugs with many side effects, we can target the disease with a specific drug."

BLOOD SUGAR BATTLES

AS DIABETES CASES MULTIPLY, DUKE CAREGIVERS ARE MOBILIZING IN NEW WAYS TO KEEP THE DISEASE UNDER CONTROL—IN THE HOSPITAL AND OUT

BY ANGELA SPIVEY

IT'S 2:15 ON A FRIDAY AFTERNOON, AND MEMBERS OF DUKE'S DIABETES MANAGEMENT SERVICE HAVE BEEN ROUNDING IN DUKE UNIVERSITY HOSPITAL FOR ABOUT AN HOUR. ATTENDING ENDOCRINOLOGIST SUSAN SPRATT, MD, ENDOCRINOLOGY FELLOW LEONOR CORSINO, MD, AND RESIDENT ERIN VAN SCOYOC, MD, WORK THEIR WAY THROUGH A LONG LIST OF PATIENTS. THEY WILL VISIT EVERY FLOOR OF THE HOSPITAL, FOR MOST OF THE AFTERNOON. THEIR SINGLE-MINDED MISSION—CONTROLLING BLOOD GLUCOSE LEVELS.

At each stop, the team gathers outside the patient's door, checking the latest numbers in the chart. They make a continual effort to reach equilibrium between the food the patient is eating, any tube feeds, the short-acting and long-acting insulin administered, and each patient's sensitivity to it.

At one stop, Spratt and Corsino debate just how many calories a patient has consumed, based on notes in his chart and their own observations. "When we visited he was just getting a puree, green beans," Corsino says. "No, he was eating a lot when I came back from rounds," Spratt exclaims.

They check his latest blood glucose reading; it's a bit low. "We need to back off," Spratt says. They will reduce his dose of short-acting insulin because he may not be eating all of his food.

It is this way at each stop: reviewing the numbers, a strategy session, doing the math, and then—a decision. More and more such small battles are happening every day, both inside the hospital and in Duke's outpatient clinics, as caregivers struggle to defend patients against an enemy that gains ground with each passing year.

Mark Feinglos, MD, has seen the relentless advance of diabetes from the front lines. Currently chief of the Division of Endocrinology, Metabolism, and Nutrition, he founded Duke's Diabetes Management Service 20 years ago, when diabetes was not nearly as common as it is today. While type 1 diabetes, in which the body produces no insulin at all, has remained relatively rare, cases of type 2 diabetes—associated with obesity and inactivity—have exploded as America's population becomes increasingly sedentary and overfed. According to the Centers for Disease Control, the percentage of North Carolinians who report being diagnosed with type 2 diabetes has nearly doubled in just the past decade, rising from 4.5 percent of the population in 1995 to 8.5 percent in 2005.

The epidemic is hitting the community hard—and complicating care in almost every medical specialty. Feinglos estimates that at least 15 to 20 percent of patients in Duke University Hospital today have abnormal glucose. That's a problem, since high blood glucose impairs white blood cell function, making those patients more vulnerable to infection. Moreover, Feinglos points out, "There are now clear data, at least in intensive-care-unit settings, that having lower glucose decreases morbidity and mortality."

As a result, the Diabetes Management Service finds itself busier than ever, with consult requests coming from almost every area of the hospital. "The level of blood sugar that raises eyebrows has changed," Feinglos says. "In the past, other services might not have bothered to call us—they might have handled it themselves—unless glucose was at least twice normal. Now we might get a call at 50 percent above normal." The team has expanded to meet the demand, even stationing endocrinology nurse practitioners on two other services—cardiology and cardiothoracic surgery—full-time.

The team also stands sentry against elevated glucose even in patients not previously diagnosed with diabetes. Sometimes, just the stress of being sick can cause a temporary increase in blood sugar. But because so many people have undiagnosed diabetes, Duke physicians now try to get to the bottom of such fluctuations by checking a hemoglobin A1C, which is a marker of average blood glucose over three months. Even if patients don't turn out to have diabetes at present, those stress-related increases in blood sugar could be a marker of things to come. Research from Duke's Richard Surwit, PhD, and Feinglos suggests that people whose blood glucose is easily perturbed by stress are more likely to go on to develop diabetes. "Many of these folks, even if their hyperglycemia is worse because of stress, probably have some underlying glucose impairment," Spratt says. "The sooner we can target that, the better off they'll be."

ON PATROL: ATTENDING ENDOCRINOLOGIST SUSAN SPRATT, MD, AND ENDOCRINOLOGY FELLOWS LEONOR CORSINO, MD, AND BRYAN BATCH, MD (LEFT TO RIGHT) DISCUSS A PATIENT'S GLUCOSE LEVELS DURING THEIR REGULAR ROUNDS. WITH UP TO 20 PERCENT OF PATIENTS IN DUKE UNIVERSITY HOSPITAL NOW SUFFERING FROM ABNORMAL GLUCOSE, THE DIABETES MANAGEMENT SERVICE'S CASELOAD HAS ROUGHLY DOUBLED OVER THE PAST THREE YEARS.

PATROLLING THE WARDS

As the diabetes management team troops from floor to floor, they are joined by Sarah Gauger, the endocrinology nurse practitioner who has been stationed on the cardiology unit permanently since last year. Her colleague, endocrinology nurse practitioner Jonathan Warren, has a similar role on the cardiothoracic surgery service. Fueling those assignments were Duke data showing that tighter glucose control results in lower rates of mediastinitis—a life-threatening infection of the mediastinum, the chest cavity that contains the heart. The efforts have resulted in faster recovery times as well: "The Diabetes Management Service has shown that just by getting us involved on day one of hospitalization, rather than day three or four, we decrease the length of stay for patients with diabetes on the cardiology services by .6 days—more than half a day," Spratt says.

Corsino says that she and the other fellows learn a lot from the nurse practitioners, who spend most of their days conducting the balancing act it takes to achieve the right combination of food and insulin that will add up to normal blood glucose levels. To help house staff and nurses navigate this territory, Spratt, nurse practitioner Melanie Mabrey, and Lillian Lien, MD, have developed protocols for determining insulin dose, and when to use subcutaneous versus intravenous insulin.

Their protocol for dosing IV insulin, for instance, uses multipliers that reflect how much insulin the patient is already receiving, rather than increasing the dose in set amounts. In a small study published in 2005 in *Endocrine Practice*, the team found that the protocol reduced errors and improved glucose control compared to an older method. "We are continuously updating our protocols and trying to improve our teaching of house staff and nurses," Spratt says.

ENLISTING HELP FOR THE COMMUNITY

If managing diabetes in the hospital requires a small army of doctors, nurse practitioners, and nurses, how can a person do it at home? It's not easy. Many have to monitor their glucose levels several times a day, interpret the results, and use the data to adjust their dose of insulin and other medications.

But even harder than all that, for many people, is changing what they eat. "Without an appropriate diet, there is no medication that will work," Feinglos says. "That's why this is so difficult to do. Because giving people medications is easy. Altering lifestyles is hard."

Why is diet so crucial? "Diabetes is basically a fuel-distribution problem," Feinglos says. "If you have a problem processing fuel, and you put too much fuel through the line, you flood the engine."

Normally, the body breaks food down into glucose (sugar). The hormone insulin helps transport glucose inside the muscles and cells, where it can be converted into energy to power a 30-minute walk on a treadmill or 15 minutes of vacuuming.

But in type 2 diabetes, either not enough insulin is produced by the beta cells (insulin-producing cells in the pancreas), or the muscles and other tissues aren't as sensitive to insulin as they should be, so they don't take in the glucose they need. Then the excess sugar is left to circulate in the blood, over time causing damage to the eyes, the kidneys, the nerves.

"WITHOUT AN APPROPRIATE DIET, THERE IS NO MEDICATION THAT WILL WORK [TO CONTROL DIABETES]. THAT'S WHY THIS IS SO DIFFICULT. BECAUSE GIVING PEOPLE MEDICATIONS IS EASY. ALTERING LIFESTYLES IS HARD."

—MARK FEINGLOS, MD

Medications can improve insulin secretion and insulin sensitivity. But if the patient doesn't also watch his or her diet, the enhanced glucose transport can actually exacerbate the problem, Feinglos says. "If you don't control the caloric intake, then all you're going to do is facilitate transport of the extra calories, which means they're going to be stored, which means you're going to gain weight. This contributes to the problem, because it makes insulin resistance worse.

"You see that notoriously: people come in and their sugar's uncontrolled, and you start them on medication, and six months later their sugar is still not very well controlled, but they weigh about 50 pounds more. That's a terrible problem," he says.

Dietary recommendations vary depending on whether a patient has type 1 or type 2 diabetes, their weight, and what other chronic conditions they must manage. "For patients with type 2 diabetes, who are often overweight or obese, learning how to decrease calories, control portions, and eat a balanced diet is very important," Spratt says. "Our concept of portion size is very skewed—to a lot of people, super-size looks normal."

MEDICATIONS COMPLETE THE ARSENAL

While managing diet is the first line of defense, Feinglos points out that medications have to be added early. In theory, diet and exercise can completely control diabetes in some patients. But, in the real world, most people find it's just too hard.

And waiting can be dangerous. "The problem with a damaged beta cell is that if you keep stressing it, it's going to get more damaged," Feinglos says. "Even slightly high glucose causes you to put out more insulin, and if you're continuing to tell this damaged beta cell, 'do it, do it, do it,' it's going to run out. It's like spending the principal in your bank account."

WHAT'S SO BAD ABOUT EATING TOO MUCH?

DUKE RESEARCHERS ARE LEARNING MORE ABOUT THE LINK BETWEEN OBESITY AND DIABETES—AND BELIEVE THE STARTLING RESULTS OF GASTRIC BYPASS SURGERY MAY PROVIDE NEW CLUES

Type 2 diabetes is known to be associated with obesity, but it's not clear exactly why. Some explain it this way: obesity itself may not cause diabetes, but the behaviors that lead to weight gain—taking in too many calories and burning too few—probably do.

A few years ago, research from Duke's Richard Surwit, PhD, Mark Feinglos, MD, and colleagues showed that in a particular strain of mouse which is genetically predisposed to diabetes and obesity, those who ate a high-fat diet went on to develop diabetes, while those fed a lower-fat diet did not—even when eating the same number of calories.

Now basic research from Duke's Sarah W. Stedman Nutrition & Metabolism Center is beginning to suggest why. Basically, an overload of the byproducts created during fat metabolism can damage the machinery that regulates insulin sensitivity and production. "We think that part of how insulin resistance comes about is that the muscle begins to inappropriately accumulate lipids and byproducts of lipid metabolism," says Stedman Center director Christopher Newgard, PhD.

The scientists are also starting to see that overloading on fat can lead to reduced secretion of insulin. "We can show in our cellular models that if you bombard insulin-secretion cells—islet cells—with elevated fat, for a couple of days for example, then you can see an impairment in insulin secretion." The researchers are currently working to pinpoint exactly which lipid-derived metabolites are the culprits, he says.

The researchers are also finding that an overload of all the nutrients, not just fats, is probably what's wrong with the typical American meal of a fast-food sandwich, fries, and a soda. Their work suggests that byproducts of metabolizing too much protein, for instance, can have bad effects as well. "That hamburger has protein in it too, and the 32-ounce soft drink has a ton of carbohydrate in it," Newgard says.

Christopher Newgard, PhD

Newgard is also in the very early stages of studying, in collaboration with Eric DeMaria, MD, chief of endosurgery, and Laura Svetkey, MD, director of clinical research at the Stedman Center, why patients who undergo bariatric surgery show improved insulin sensitivity very quickly—within two to four weeks. [A 2004 meta-analysis published in *JAMA* found that over time diabetes was completely resolved in 76.8 percent of patients who underwent bariatric surgery.]

The pancreas was once thought to be the primary producer of hormones that regulate metabolism, but now scientists know that fat tissue itself as well as the gastrointestinal tract makes hormones that regulate energy balance and appetite. "So if you've rerouted the stomach and the intestinal system through bariatric surgery, it stands to reason that you may have altered the production of hormones that are normally produced in the gut during food ingestion," Newgard says. If this is really what's happening, he, DeMaria, and Svetkey want to find out exactly why. To do so, they will measure metabolites and other markers in patients both before and after bariatric surgery, and compare them to patients who lose weight by other means.

"We think this is going to be a very exciting model for understanding biochemical changes that drive improved insulin action," Newgard says.

MARK FEINGLOS, MD

Subcutaneous insulin is still the backbone of treatment. Short-acting insulin is now available in an inhaled form, which could be used as a complement, though it takes some training for patients to use it correctly, Feinglos says. (A CME/CE activity covering inhaled insulin is available online at www.medscape.com/viewprogram/5726.*)

For some patients, enhancing the body's sensitivity to their own insulin with oral drugs such as metformin is enough. "I think the best drug for type 2 diabetes is still metformin because it isn't associated with weight gain, and it attacks several of the problems of type 2 diabetes—insulin sensitivity changes, and production of glucose by the liver," Feinglos says.

A new class of drugs, DPP-4 inhibitors, prevents the breakdown of a hormone that enhances insulin secretion. These drugs can be taken orally and have the happy side effect of decreasing appetite in some people. The first of this class, Januvia (sitagliptin), is now on the market. "If they really do increase insulin secretion and are not associated with weight gain, and maybe cause a little weight loss, they should be quite popular," Feinglos says.

MOBILIZING IN THE COMMUNITY

An individual doctor's office can find it almost impossible to do all that's needed to take care of a patient with a chronic disease such as diabetes. Feinglos says he can spend almost an hour studying a particular patient's lab results, trying to tease out the reasons why blood sugar is still not well controlled. Most community practitioners don't have that kind of time. And, adds Lloyd Michener, MD, chair of the Department of Community and Family Medicine and director of the Duke Center for Community Research, because many patients with diabetes have to make fundamental changes in their lives, a lot of patient education has to happen. "Doctors, with all due respect to us, aren't always the best at educating about lifestyle change."

So Duke and 21 other institutions nationwide are changing the way they offer care for chronic disease, through the Robert Wood Johnson-funded Academic Chronic Care Collaborative (ACCC). Members of the collaborative try different strategies for managing chronic diseases such as diabetes, then evaluate the outcomes. Individual practices use the data to measure how well they are caring for patients, and the data are also shared among practices in the collaborative so that they can learn which aspects of the model are working.

"We're trying to make sure that everyone in our practices is getting better," Michener says. "We're making steady improvement, and we're comparing our practices to some of the best practices in the country."

To develop more effective ways of delivering care, "We looked at our whole process starting from how you call for an appointment, to what information patients want, and redesigned our system to try to provide that," Michener explains. "Traditionally, we've left it to people to call us to tell us when they need to be seen, and they're seen one at a time, the patient and the doctor in the office." But with the chronic care model, a team of caregivers such as physician assistants, nurse practitioners, social workers, health educators, physical therapists, and nutritionists work together to help patients take a more proactive role in their health.

For example, as part of the ACCC efforts, patients with diabetes in Duke community clinics are encouraged to attend monthly Diabetes Group Visits. Each 90-minute session includes a class on some aspect of diabetes care, as well as time for discussion. Patients are much more likely to ask questions of a nurse, health educator, or even another patient than they are a doctor, Michener says.

*Reference provided for information only; this activity is not sponsored or endorsed by Duke Medicine.

Editor's note: At press time a study in the *New England Journal of Medicine* (May 21, 2007) linked the diabetes drug Avandia (rosiglitazone) to increased heart attack risk. Visit dukemedmag.duke.edu to read a letter to patients from Duke General Internal Medicine on the issue.

AS THE DIABETES EPIDEMIC SWELLS, DUKE CAREGIVERS ARE EXPANDING THEIR EFFORTS FROM WARDS AND CLINICS TO APARTMENT COMPLEXES AND COMMUNITY CENTERS, OFFERING A VARIETY OF CLASSES, SUPPORT GROUPS, AND EVEN IN-HOME CARE MANAGEMENT SERVICES TO HELP PEOPLE KEEP THEIR DISEASE UNDER CONTROL. FOR INFORMATION ON MANY OF THESE PROGRAMS, VISIT COMMUNITYHEALTH.MC.DUKE.EDU.

On one such Tuesday night, six people attend the Diabetes Group Visit at Duke's Family Medicine clinic. Exercise physiologist Michelle Mosberger talks to the group about ways to get more activity into their routine. She shows them simple exercises they can do in a chair while watching TV, such as arm or leg lifts. Participants ask whether walking a few extra trips to the copier at work or parking farther away at the grocery store really counts. "Absolutely!" Mosberger says. "Every little bit helps."

During the class, participants slip out for a mini-exam, in which a physician's assistant takes vital signs, measures glucose levels, and reviews medications.

The participants get especially engaged when it's time to just talk. "It's a good place to talk out loud, no matter what you say or how stupid it may sound," says Jackie Aiken, who started attending the monthly classes shortly after she was diagnosed with diabetes in September 2006.

Aiken mentions that for about two weeks she stuck to a routine of walking at night, but then lost the motivation. The mother of four would like to join a gym, to get some exercise and some "me time," but she finds memberships too expensive.

Another group member tells her that she could try walking at the mall.

An intern who's there with Mosberger tells Aiken that the YWCA offers scholarships, if you ask.

Clinical associate Sarah McBane, PharmD, answers Aiken's question about her insulin. No, she doesn't need to pack it on ice when she goes out for the day.

Another patient. The exercise physiology intern. A pharmacist. On that night, the army helping Aiken battle diabetes was made up of three. □

RX FOR DIABETES: LOOK ON THE BRIGHT SIDE

FIRST, THE BAD NEWS. OR, DEPENDING ON HOW YOU LOOK AT IT, THE GOOD NEWS. DEPRESSION DOESN'T SEEM TO AFFECT BLOOD GLUCOSE LEVELS, WHILE STRESS DOES. BUT THERE ARE SIMPLE WAYS TO DO SOMETHING ABOUT BOTH.

In a study published in the April 2007 *Psychosomatic Medicine*, Richard Surwit, PhD, chief of Duke's Division of Medical Psychology, and colleagues found that cognitive behavioral therapy—basically teaching people to see life as a glass that's half full, rather than half empty—improved depression in a group of patients with diabetes.

But treating depression did not have any effect on blood sugar control. Surwit was surprised at the results because previous research, though mixed, had suggested that depression and glucose control were linked. His own study, with Duke colleague Mark Feinglos, MD, had shown a small connection in patients with type 1 diabetes.

"I was just stunned," Surwit says. "Cognitive behavioral therapy's effect on depression was so significant, and yet there was no effect on A1C [a marker of glucose levels over time]."

Even though treating depression doesn't seem to have any effect on diabetes, it's well known, from research by Surwit and others, that stress can raise blood sugar. Stress causes the body to make more hormones such as epinephrine, norepinephrine, and cortisol, which can lead to disruptions in the body's normally tight control of blood sugar.

Richard Surwit, PhD

But cognitive behavioral therapy, as well as progressive muscle relaxation, can produce reliable decreases in these hormones. For example, in one of their earliest studies of stress and diabetes control, Surwit and Feinglos had 12 diabetes patients stay in a dormitory setting. Half of them learned and practiced progressive muscle relaxation. That group showed decreased blood sugar after only nine days, and blood samples revealed that their cortisol levels were measurably lower than the control group's.

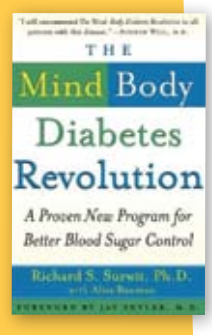
"When the patient is having trouble controlling their glucose, physicians might suggest that they monitor their blood glucose in situations where they feel they're under stress, and in situations where they feel they're not," Surwit says. "And if there's a pattern there, a physician can recommend that they do something about it behaviorally."

For instance, self-help books such as Surwit's *The Mind-Body Diabetes Revolution* can help people learn simple techniques to manage stress on their own. "The reason I did this book was, for most people, insurance is not going to pay for behavioral intervention unless there's a psychiatric diagnosis," he says.

Muscle relaxation sounds easy enough, but can people really practice cognitive-behavioral therapy on their own? Yes, Surwit says.

"We created a structured set of exercises that you can do to look at a situation, analyze it, decide whether the way you are responding is appropriate or not, and then change how you are responding if necessary.

"A lot of stress that we put on ourselves has to do with how we appraise what's going on around us," he says. For example, if your work supervisor snaps at you, you might assume that he's unhappy with you. Or, you could assume that he's just having a bad day. "People have to be able to figure out which is which. If your boss is having a bad day, that's too bad for your boss, but it's not something that should make you upset."



Lower Stress, Lower Sugar

Tips on managing stress from *The Mind-Body Diabetes Revolution*:

- **Tense, then relax.** There are different variations, but the main idea behind progressive muscle relaxation is to consciously tense one group of muscles, such as your feet or your thigh muscles, for about 10 seconds, then let them fall limp. Notice how the complete relaxation feels.
- **Practice regularly.** When performed over time, such exercises can help people sense the first signs of muscle tension, and learn to instantly relax them when feeling anxious. Surwit suggests working up to 30 daily "mini-practices" of 30 seconds each, whenever you feel your muscles feeling tense, your heart racing, or your palms sweating.
- **Observe your thoughts and test them for accuracy.** When you find yourself feeling irritated or stressed, stop and write down your mood. What thoughts led to it? Are those thoughts based in truth? List alternative beliefs and test them for accuracy as well.

THINNING A GENERATION

BY KATHLEEN YOUNT

CALL THEM GENERATION X BOX.

Our increasingly sedentary, overweight kids are in big trouble. Pediatric obesity rates have tripled since 1980, with one out of every three American children now overweight or obese. As these children develop the debilitating chronic diseases of their parents and grandparents, pediatricians are routinely encountering illnesses many of them never expected to treat—from fatty liver disease to type 2 diabetes.

It's one thing to bemoan America's expanding waistline. But with obesity making our children ill, it's not merely a social issue—it's a full-blown medical crisis. From a new childhood obesity clinic to community-based interventions, Duke caregivers are adopting sweeping new strategies to address the health of a generation.

KIDS ON DRUGS—LIKE LIPITOR

When pediatrician Sarah Armstrong, MD, left Baltimore last year, she left with a purpose. Armstrong is still early in her career, but she was already noticing a disturbing trend among patients in the inner-city clinics where she worked. "High blood pressure, adult-type diabetes, sleep apnea, cholesterol problems, early puberty," she says, ticking off a list of diagnoses she was making with increasing frequency. "Sixty percent of overweight kids are already exhibiting a clinical risk factor for heart disease."

Armstrong joined the faculty at Duke to form a new clinic, the Duke Children's Healthy Lifestyles Program, that is the first multidisciplinary clinic at the medical center devoted exclusively to caring for overweight and obese children. The program provides individual family assessments and interventions to help reverse weight gain in children and treat the medical conditions that may be developing as a result of a child's obesity.

Healthy Lifestyles fills a new clinical and research niche, by trying to catch these kids before their health problems necessitate specialty care. But it's joining an already robust array of initiatives at Duke that have been battling childhood obesity for a decade, from individual patient interventions to community-wide programs. Researchers and clinicians here say that pediatricians need to prepare to treat a mounting wave of obesity-related chronic illness. But more important, they say, there's much that doctors can be doing to help reverse the problem before it gets any worse.

TAKING IT FAMILY BY FAMILY

At the Duke Clinic on Roxboro Road, Armstrong and her staff have carved out a dedicated space for the Healthy Lifestyles Program. Within its first four months, word-of-mouth had drawn more than a hundred families to the program—most of them referred by local pediatricians, who haven't time during a typical office visit for the type of intensive intervention offered here.

A patient's experience with Healthy Lifestyles begins with a two-hour-plus evaluation by three specialists. Armstrong assesses the patient's weight-loss needs and addresses any related medical problems or health risks. A registered dietitian meets with the family to go through their entire diet history and recommend practical and healthful meal plans. A social worker screens for behavioral and emotional problems in the patient and the family (such as depression), then helps the family create healthy—and hopefully permanent—lifestyle changes.

The team doesn't use the words *diet* or *exercise*. Instead, the game is all about activity and making healthy choices. "Some kids say they don't do any activities because they don't like group sports," says Armstrong. "We help them find dancing, swimming, skating—things that they'll enjoy."

Patients leave their initial assessment with an information packet—a sort of battle plan. "We write in what their specific goals are, what their specific recommendations are, a couple of sample meal plans if that's appropriate," says Armstrong. Patients are also offered the option to continue with an intensive program of five monthly sessions that address specific lifestyle modifications. All families return for a six-month follow-up.

High Five for Healthy Families

Once a month, participants in Duke Children's Healthy Lifestyles Program gather to focus on integral—and easily attainable—lifestyle changes that kids and families can implement to achieve a healthy weight. The modifications are basic, but they can yield big results:

- Sleep right for good health
- Be active for 60 minutes a day
- Limit TV to two hours a day (or less)
- Trade sugar-sweetened drinks, sodas, and juice for water
- Eat right-sized meals with family at home

At the final session, families are presented with a new, customized cookbook, filled with all of the family's favorite recipes—made more healthful by the dietitian.

At every session, kids get a take-home toy that's also a tool for that topic—from jump-ropes and exercise bands for "active TV watching" to a pedometer for physical activity. "We just tell the kids to beat their best," says Armstrong of the exercise component. "Every night they write down how many steps they took; sometimes the parents will buy a pedometer too and the family does it together. Plus," she adds, "it looks kinda like a pager; some of the kids think that's cool."

For more information about the Healthy Lifestyles Program, visit dukehealth.org/healthylifestyles. To refer a patient, please call 919-620-5356.

For more information about Duke's community-based activity and nutrition programs call 919-681-3187 or visit communityhealth.mc.duke.edu.

FULL-FAT ENVIRONMENT

In the Healthy Lifestyles nutrition room, a shelf overflows with plateless mounds of green beans and cornflakes in search of a bowl. Rounds of cut corn and free-form grits flank tiny steaks, drumsticks, fruit—all plastic replicas in properly portioned sizes. "Most people have no idea what a single serving of bread is," says Armstrong. She picks up a plastic bagel that looks miniature but is actually the boiled bread's originally intended size—half that of your average bagel-stand fare.

Posters with positive food images decorate the walls of every room in this clinic—one displays an enticing rainbow of fresh fruits and vegetables. Healthy Lifestyles is an oasis of healthful eating advertising that looks quite different from the fast-fried world awaiting families when they leave.

Susan Yaggy, chief of the Division of Community Health, says that addressing these climate-related causes of obesity is essential to the long-term success of programs such as Healthy Lifestyles. "We have to change the environment in which kids live and work and play," she says. "Food is cultural, it's familial, it's part of religious observances in the home. Because of all that, to help a family make lasting changes, we need to bring a lot of forces to bear in a combined, collaborative effort."

Her group has devoted attention to childhood obesity since its inception in 1996. "When our division was formed, our first projects were studying asthma, and obesity was there," she says, because asthma is yet another chronic illness more common among obese kids. Her division has helped communities throughout the state to implement physical activity and nutrition programs. Many of these communities have had great success with the families enrolled, but the obesity problem in North Carolina overall continues to worsen.

"It's a problem that takes a lot of work, a lot of organizing, and a sustained effort," Yaggy says. "And those are hard." However, there are increasing opportunities now, including

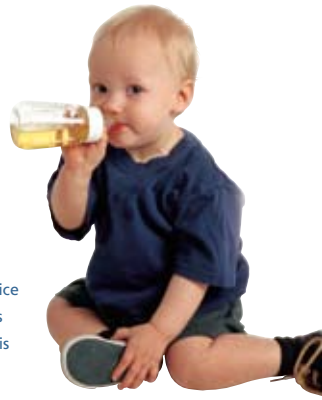
Sixteen-year-old Rachel Creel is one of the first patients to enroll in the Duke Children's Healthy Lifestyles program, directed by Sarah Armstrong, MD (right). "It can be tricky to have to tell your child to eat less," says Rachel's mother, Trish Creel. "It's not like talking to your kids about other kinds of risky behaviors, like not smoking, not doing drugs. This program gives me somewhere to go. I don't have to be the bad guy anymore."

funding for new programs, that weren't there before. "There's more willingness to use the social good of government to help people make good choices."

One example, she says, is the Partnership for a Healthy Durham, established by the Durham County Health Department—the local organization for the national Healthy People 2010 initiative. Yaggy serves as chair of its obesity and chronic disease committee. That group has created a Web-based map to help families find physical activity and nutrition resources near their home, from farmer's markets and trails to gyms and after-school programs.

The hope is that a new community infrastructure offering obesity-combating programs, exercise opportunities, and nutritious food choices will take root, slowly supplanting our well-entrenched toxic eating environment. "Research shows that multiple, reinforcing strategies—not single interventions—are what work to help patients and families make long-term changes in their health behaviors," Yaggy says. "So when a parent walks out the clinic door with his child, they should know about healthful options, whether it's at the parent's workplace or the child's school or weekend events at church, to support changes that they make at home. That kind of community support is needed to reinforce your decision to change your family's health behaviors."

Rachel Creel's blood pressure was high when she began the Healthy Lifestyles program, so the team based her nutrition plan on the DASH diet, shown to reduce hypertension as well as cholesterol and weight. Compared to other programs she's tried, Rachel says what she has learned through Healthy Lifestyles feels doable. "Salads are my favorite thing," she says. "But my problem was that I loaded on the dressing. Now I know to make smaller salads, so I can enjoy the amount of dressing I like and not overdo it." Rachel also started eating regular breakfasts to curb hunger throughout the day, and her dad, Chuck Creel, moved a television into the family's home fitness room, which she says makes exercising more attractive. But her biggest inspiration is the Healthy Lifestyles staff. "They're all so upbeat," says Rachel. "And they never use the words diet *or* exercise." *"It's really refreshing," agrees her mom, Trish Creel. "They talk about activity and nutrition instead. So it doesn't seem like an obligation, but an opportunity to be healthy."*



Duke dietitian Gwen Murphy makes calorie-dense drinks like soda, sweet tea, and even fruit juice her first target when she works with kids struggling with obesity. "Some kids drink liters of this stuff every day," she says. "If I can get them to switch to water, milk, or diet drinks, that alone is often enough to stop weight gain."

HAVING "THE TALK" WITH FAMILIES

Often, Yaggy says, a key trigger for a family to make that decision is a physician expressing concern about a child's weight. But according to Duke's director of adolescent medicine, Terrill Bravender, MD, MPH, many pediatric practices don't even chart their patients' body mass index (BMI). "Pediatricians think they can identify a child who's overweight by looking at that child, but that's simply not true," he says. "The normal BMI for adults is static; you're overweight with a BMI of 25, and obese at 30. For children what's 'normal' changes from year to year."

Many pediatricians also report feeling uncomfortable discussing children's overweight with their parents. "Some parents are shocked when you bring it up," says Bravender, because for so long obesity has been considered a private, cosmetic, even moral issue more than anything else. Physicians, says Bravender, can be pivotal in changing the conversation to one based on health. "That's why we're talking about it, after all," he says. "I don't care if my patient is overweight, if that individual is healthy. There's always a wide variation in what's 'normal,' and frankly if a kid looks like he's genetically determined to be in the 90th percentile for weight but he's active and doesn't eat poorly, I'm less concerned about that child. It's the health implications that I'm worried about.

"My father smoked when I was young," he says, "and I remember he went to the doctor and the doctor didn't mention his smoking. So my dad's take-home message was, 'Well, I guess I don't smoke too much because the doctor didn't say anything.' And I think it's the same with obesity. If you don't say anything, many patients and parents interpret that as tacit approval."

Bravender calls our culture an obesigenic one, noting our dependency on cars for transportation and the sedentary style of much of our work and entertainment. "It's very easy—even for kids—to make it through the day without expending any physical energy at all." Combine that with the expansive variety of pre-prepared, readily available food, the cheapest of which is generally the most nutrient-poor and calorie-dense. "I tell my patients all the time," he says, "that when you think about it, it's really no surprise that we have an obesity epidemic."

DIETS DON'T ALWAYS WORK

Perhaps the ugliest fact about the pediatric obesity epidemic is that lifestyle modification, as a strategy for lasting weight loss, often fails. That's because, as evidenced in many behavior-related diseases, it's extremely hard for people to permanently change entrenched patterns of behavior. Pediatric endocrinologist Michael Freemark, MD, says that's why it is incumbent upon pediatricians to try to prevent overweight and obesity before it emerges.

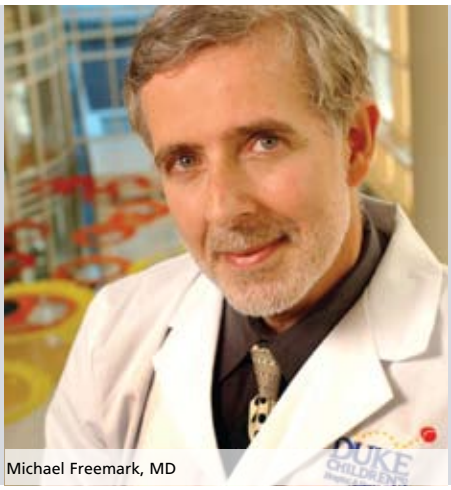
Freemark has overseen Duke's Pediatric Insulin Resistance Clinic since it was established 10 years ago. He says that this patient population has not only swelled, but also worsened in health status. Meanwhile, pediatric obesity remains a phenomenon that's poorly understood—which is why Freemark has taken the helm of the Healthy Lifestyles Program's research component. He'll coordinate studies with Armstrong's clinic to better understand the disease's etiology, prevention, and treatment.

Studies will aim to characterize the metabolic function of obese mothers and their babies, to learn at the physiologic level how to identify the children at greatest risk for excess weight. "For the highest-risk group, we could intervene more aggressively and earlier," he says. Among the interventions that will be studied in these very young children is banning sugar-sweetened beverages for infants born into high-risk families. "We want to determine whether eliminating those sugary drinks right from birth can prevent weight gain within the first two years."

HELP IN A PILL?

For the legions of children who are already obese, Freemark's group is exploring what weight-loss medications might be safest and most effective to use in children. Studies by Freemark and other investigators suggest that metformin, a drug developed to treat type 2 diabetes in adults, can be useful in helping obese adolescents with impaired glucose tolerance, severe insulin resistance, or polycystic ovary syndrome. Among drugs used to treat obesity, metformin likely has

Terrill Bravender, MD



Michael Freemark, MD

Should weight-loss medications be used in children and teens? Duke's Terrill Bravender, MD, and Michael Freemark, MD, have different takes on the issue, but they agree on a key point—as Bravender puts it, "We need to find a safe and effective medical treatment for this condition, because there is no behavior modification that consistently works."

the fewest side effects and the best benefit-to-risk ratio. Other medications approved for treatment of obesity, including orlistat and sibutramine, may cause diarrhea and hypertension, limiting their use in the general population. Freemark and his colleagues will study metformin's usefulness in preventing problems in overweight children who are at highest risk for developing type 2 diabetes and fatty liver disease.

Freemark notes that early weight-loss drug intervention is a topic of much debate. "A lot of people are not wild about the idea," he says. "They believe that only lifestyle interventions are justified until major complications have developed. I've argued that medications may be considered if pre-diabetic conditions persist despite a good-faith effort at lifestyle change."

Freemark explains that the debate stems from the many questions that need to be answered about the effects of anti-obesity drugs in still-changing bodies. He thinks it often comes down to the particular patient one sees in the clinic. "Everyone agrees that lifestyle intervention should be initiated before drug therapy and should be maintained during and after such therapy if possible," he says. "But if my patient has multiple family members with type 2 diabetes and early-onset cardiovascular disease, and the kid has been obese and insulin-resistant despite lifestyle counseling, my feeling is, it's justified to try to do something more. But this idea is not accepted by everyone."

BABY STEPS TO BETTER HEALTH

Bravender would count himself among those who are more leery than Freemark of using drug therapies in obese children. But he does agree with Freemark in the most important way: "We need to find a safe and effective medical treatment for this condition," he says, "because there is no behavior modification that consistently works." He thinks this behavioral failure speaks to the level of pathology in the environment around us, as well as the intense, inborn drive to eat. "There's nothing more basic than the needs to eat and drink to survive," he says. "When you're surrounded by food, what else are you going to do?"

But then what exactly do you do about a disease whose etiology is rooted in our most fundamental impulses? Yaggy says the solution needs to come from an evolution in our overall culture. "It won't just be one clinic or one community program," she says. "It needs to be an interrelated community, government, medical, and family enterprise." In short, she says, the issue of obesity must, like smoking, become something "that's civic, not something seen only as a personal responsibility and a personal failure."

Armstrong echoes that sentiment. "In this country there are a lot of organizations working on the problem of childhood obesity," she says, "but they tend to

operate in silos." She hopes that the Healthy Lifestyles Program will be something that doctors throughout North Carolina will be able to use and replicate in their own communities.

Armstrong notes that the program is little more than a toolkit to help inform and equip individual families to make healthy choices. "Only they can do it," she says. "We can make the recommendations, but it's totally the determination of these folks—that they want their kids to be healthy." And the changes affect more than just the kids—the health of the whole family improves. "For some of these parents, changing their lifestyle habits for themselves wasn't enough, but now they want to change it for their children. The kids become the inspiration they needed." □

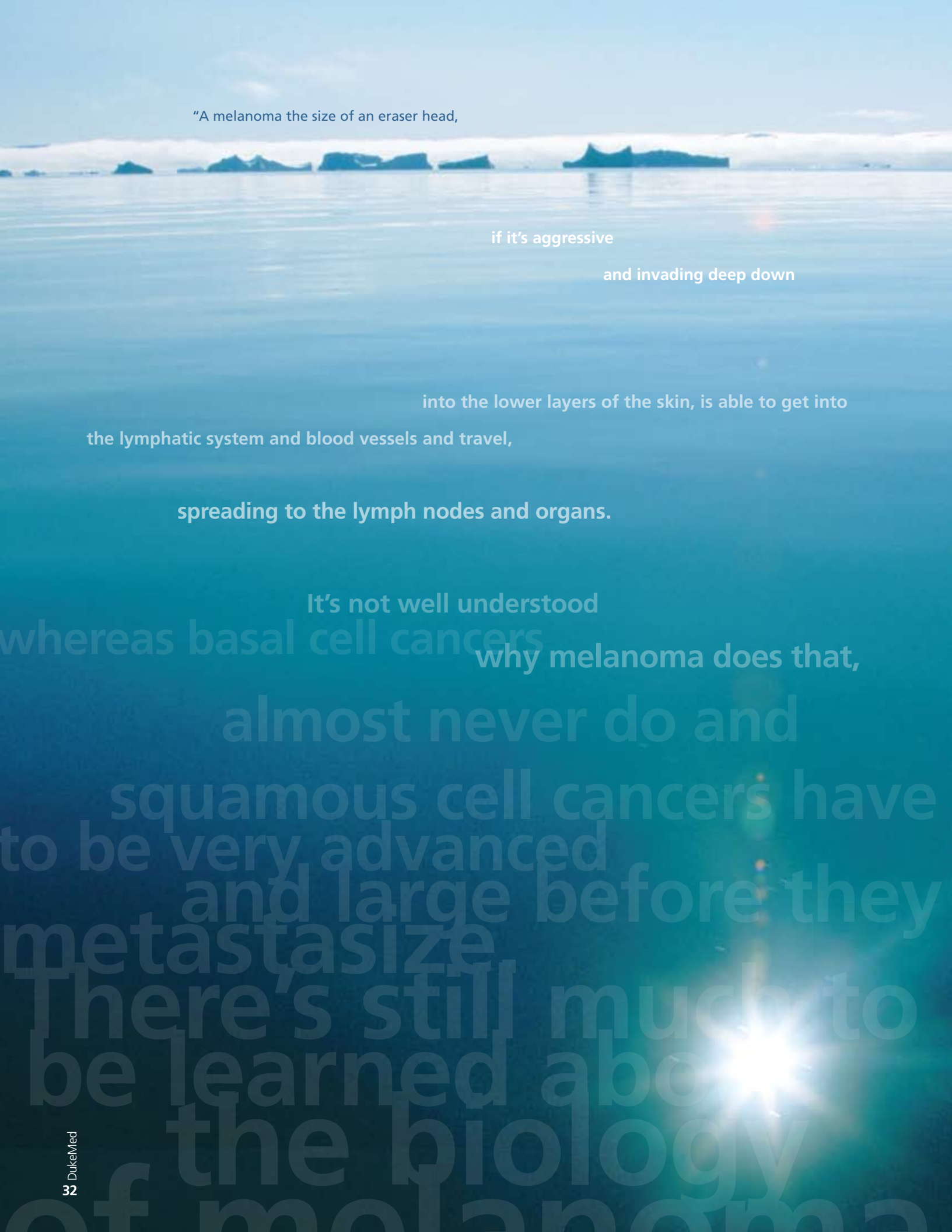
Overfed but undernourished

Many obese kids are also malnourished—their caloric intake is not only excessive, but also nutrient-poor. This could be because so many of our lowest-priced foods are also our least healthful. That's the epidemic's ironic twist: this disease of surfeit strikes disproportionately among the poor.

And like most other chronic illnesses, it runs rampant in these communities that often have fewer resources with which to combat the problem. Low-income neighborhoods generally have few large grocery stores and instead have to rely on quick marts; lean cuts of meat and fresh fruits and vegetables are often unavailable, and if available are expensive compared to canned goods. And in some neighborhoods, it's often simply safer to keep kids indoors, even if it means they are less active.

Sarah Armstrong, MD, says that in the Healthy Lifestyles Program, the families who have struggled the most to implement healthy changes are those also dealing with issues such as homelessness and poverty. Duke dietitian Gwen Murphy notes that a scarcity of healthy food can be a major contributor to overeating and to eating unhealthy, calorie-dense foods. When she discusses the many community nutrition programs she works on in the Division of Community Health, poverty is often an underlying theme. One such program sends kids home on Fridays with their backpacks full of fresh fruits and vegetables. "A person who worked on that program told me that one day he watched a child sit down and eat all the food in his backpack before he even left school," Murphy says.

Read more about the many community programs and funding opportunities to combat poverty-related obesity on the division's Web site: communityhealth.mc.duke.edu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and large before they
metastasize.
There's still much to
be learned about
the biology
of melanoma

BENEATH THE SURFACE

DELVING INTO MELANOMA'S MYSTERIES

BY JUNE SPENCE

A healthy, sun-kissed glow! A safe alternative to sunlight! No harmful UVB rays!

False reassurances like these from tanning salons enrage Jane Caddell. Though her sun exposure increased a bit when Caddell moved to North Carolina from Maine, she feels certain it was the indoor tanning beds she began frequenting in her late thirties that spurred her life-threatening melanoma. For about a year and a half, she'd go with friends from work three or four days a week, sometimes dozing through the lunch hour in the warmth of the glowing bulbs.

"Of course, I'm blond-haired and blue-eyed, which makes you a little more susceptible," says Caddell. "But I just had no clue, no education on skin cancer whatsoever."

When a new mole appeared on the back of her knee, however, she took notice. "I really focused on this mole. I could tell there was some activity with it. Then it started to bleed a little bit. That gave me a sense of urgency, so I made an appointment with a dermatologist."

Caddell was diagnosed with melanoma, the rarest but most deadly form of skin cancer. "He took out a silver-dollar-sized area of skin," she recalls, "and said the borders came out clear, so he reassured me that I had nothing to worry about."

Indeed, treatment at an early stage can often stop melanoma in its tracks. According to the American Cancer Society, around 83 percent of melanomas are diagnosed at a localized stage, meaning they have not spread beyond the outer layers of the skin. In these cases, the average five-year survival rate is 98 percent.

Even when combated at its earliest signs, however, melanoma still has the potential to spread or recur. "A melanoma the size of an eraser head, if it's aggressive and invading deep down into the lower layers of the skin, is able to get into the lymphatic system and blood vessels and travel, spreading to the lymph nodes and organs," says Jared Gollob, MD, director of the Biologic Therapy Program at Duke University Medical Center. "It's not well understood why melanoma does that, whereas basal cell cancers almost never do and squamous cell cancers have to be very advanced and large before they metastasize. There's still much to be learned about the biology of melanoma."

Researchers and clinicians at Duke's Melanoma Clinic are seeking to unlock the secrets of this aggressive cancer and thereby uncover more ways to combat it—a goal becoming more urgent as the number of melanoma diagnoses continues to creep upwards, now nearing some 53,000 new cases annually in the United States alone. Each year more than 500 of those patients travel to the Melanoma Clinic at Duke, rated one of the leading specialty clinics in the United States. By providing the latest in detection and treatment, including access to experimental therapies, Duke aims to help patients in the early stages make the strongest possible first strike against the disease—and offer those with advanced melanoma more options than ever before.

"This disease is too fast, too furious—it's too big not to be in the hands of someone who can offer you all the options," says Jane Caddell, who was treated for stage IV melanoma. "At Duke, all the knowledge is under one roof. There's hope here."

AS LUCK WOULD HAVE IT

"I thought I'd been lucky," says Caddell of her initial brush with melanoma. About a year after Caddell's mole was removed, however, she developed a bronchial infection with a low-grade fever. Even with antibiotics, the fever continued, and she developed a "relentless, croupy cough" that plagued her day and night.

A chest x-ray indicated pneumonia, but it also revealed something far more menacing—shadows. A CT scan showed nodules on her lungs, her liver, and the lymph nodes in her chest. One tumor had encircled her esophagus.

"An oncologist told me that my melanoma was in stage IV," recalls Caddell. "I said, 'Well, how many stages are there?' He said, 'There's four.'"

"Stage IV refers to the fact that the melanoma has already spread to other organs or to new places in the body, far from where it started, and is usually no longer curable with surgery," explains Gollob. "High-dose interleukin-2 [IL-2] is what we give to patients with stage IV melanoma who are healthy enough to tolerate the severe side effects, for it remains the only treatment that can actually cure a small percentage of these patients."

Gollob says Duke is among a limited number of centers in the country that can offer high-dose IL-2 therapy. "It requires very intense monitoring, specialized nursing, specialized physician care, and patients have to be well enough to be treated."

IL-2 hyperactivates the immune system, explains Gollob, so the symptoms can be severe, "like what you might get if you had a serious blood infection—fevers and chills, low blood pressure, the heart rate can speed up, fluid may leak into the lungs, kidneys may temporarily shut down, blood counts go down, liver function can be compromised. We have to pay very close attention during treatment so that we know when to pull back. It sounds harsh, but put it in perspective: the average life expectancy for someone with stage IV melanoma is less than a year."

"The stuff kicks your butt," confirms Caddell, who was treated with IL-2 under Gollob's care after her oncologist referred her to Duke. "It was a bit like having entirely too many drinks and the flu at the same time. After each treatment I felt like I'd just challenged the heavyweight champion of the world, I was so battered. One of the amazing things about this treatment, though, is how quickly you can rebound from it after it stops. It's tough but doable."

Caddell's tumors shrank in response

Jared Gollob, MD, directs the Biologic Therapy Program at Duke—one of about 30 places in the country that offer high-dose interleukin-2, the only therapy to date with the potential to cure advanced melanoma or kidney cancer.

to the intensive treatment, and in June of 2006 she was told she was in remission and disease-free. She has since become an advocate for melanoma education and prevention through the organization she founded, Operation Sun Shield (operationsunshield.org).

SCRATCHING THE SURFACE

The successful outcome of Caddell's treatment is cause for celebration, but she's among only 5 percent of patients with late-stage melanoma for whom IL-2 provides a cure. Hope for greater numbers may lie in combination therapy, the focus of Gollob's research.

"We use drugs with some track record in melanoma, like high-dose IL-2 or alpha interferon [standard therapy for stage II or stage III melanoma] and combine them with new drugs that might be able to make them work better," says Gollob. Among his new phase-two trials now open to patients at Duke is one that involves what animal researchers call "chemo-switch," an approach that begins with biochemotherapy—a combination of IL-2, alpha interferon, and three chemotherapy drugs.

"We know that this combination can shrink tumors in melanoma; the problem is the tumors don't stay shrunk," he explains. But after reducing the tumors with biochemotherapy, the treatment "switches" to a combination of two other drugs: sorafenib, an experimental antiangiogenic drug approved for kidney cancer but not yet for melanoma, and a very low daily dose of temozolomide, a chemotherapy agent. "This appears to be a potent way of jumping on the tumor once it has begun to shrink. There's evidence that by giving those two drugs together like that once you've begun to shrink the tumors with the 'big-gun' chemotherapy, you can get the cancer into durable remission in animals. We hope to see it do the same in humans."

For patients with late-stage melanoma, who have no chance of a cure with surgery alone, Gollob says such trials offer additional treatment options to the current standard of high-dose IL-2 therapy. "The fact that the standard is still a long shot makes us feel comfortable saying let's try something different, using drugs that may have the potential to help in a meaningful, long-lasting way."

SHOOTING FOR MORE EFFECTIVE VACCINES

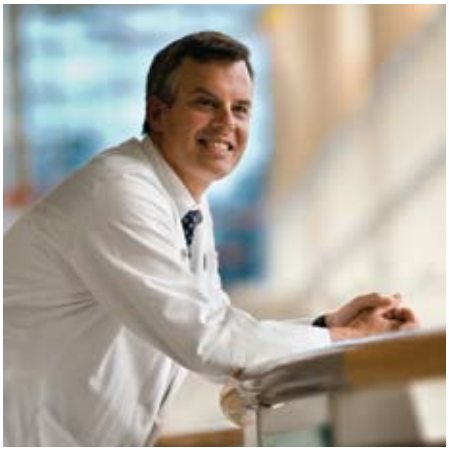
Duke is considered a leader in the field of immunotherapy, another tactic with the potential to help patients with late-stage melanoma. The founder of the Duke Melanoma Clinic and a pioneer in melanoma research and care, Hilliard F. Siegler, MD, began studying melanoma tissue antigens in 1968. His legacy continues in Duke's enduring quest to perfect a vaccine to treat melanoma.

"The body can have an immune response to melanoma," says Scott Pruitt, MD, PhD, a surgical oncologist whose research focuses on melanoma vaccine development. "But our immune response is designed to fight infection rather than cancer, so there are hurdles to overcome. Cancer cells are so close to normal cells, and there are a variety of control mechanisms in our bodies to prevent us from making immune reactions against our own antigens. One way to get around that is to get rid of those regulatory cells; another way is to more effectively direct the immune response against the appropriate targets. Ultimately we'd like to combine the two approaches."

Toward that end, Pruitt is studying an immunotherapy protocol that involves regulatory T-cell depletion. "Regulatory T-cells dampen the immune response," he explains, "so if we can remove those cells from the body, we hope to boost a more vigorous response against melanoma."

He's also pursuing an immunization protocol involving dendritic cells loaded with melanoma antigen RNA. "We think that altering the dendritic cell will generate T-cells that are more effective against melanoma."

Ideally, immunotherapy would be used to treat all patients with melanoma, "but that's way down the road," cautions Pruitt. "Our focus right now is on patients with metastatic disease." Successful vaccine protocols over the past two decades have been shown to induce a clinical response in about 5 percent of patients with metastatic melanoma. "That's just enough response to give us hope that we can keep working to overcome these regulatory mechanisms, get the right targets, and make more headway. We're continually trying to come up with a better understanding of the regulatory mechanisms of the immune system and get the next big breakthrough."



Scott Pruitt, MD, PhD, is developing vaccines against melanoma.

"A RASH OF CANCER"

Sometimes when melanoma recurs, it does so as multiple nodules located between where the primary tumor was and the regional lymph nodes. "If there are only one or two nodules, you can surgically excise them," says Doug Tyler, MD, surgical oncologist, "but sometimes there will be hundreds of nodules, almost like a rash of cancer, and you can't really remove that short of an amputation." For patients experiencing local or regional recurrences in their extremities, Tyler's specialty, regional therapy—the treatment program he established at Duke—may be the best defense.

Regional therapy allows much higher doses of chemotherapy than could be tolerated systemically. During infusion, the limb's circulation is cut off from the rest of the body, which helps to minimize chemotherapy's side effects. "The extremity can get a dose of chemotherapy 10 times greater than you could give someone by mouth or in a vein," explains Tyler. "The regional therapies are associated with about a 50 percent chance for complete disappearance of the disease, which is much higher than is seen with any systemic treatment." The procedure has become far less invasive as it has evolved, no longer requiring incisions or the use of a heart-lung machine, and Tyler is seeing similar response rates.

Building on this regional therapy model, Tyler and colleagues are designing trials that combine both regional and systemic approaches. The strategy involves first giving a targeted therapy—a drug targeting a specific protein that that may be abnormally expressed in a tumor cell—to the whole body. Targeted therapies can be introduced systemically because they usually don't have many side effects. In the middle of that treatment, the regional chemotherapy is introduced.

"Systemic treatments seem to make the tumor cells much more sensitive to the high-dose regional chemotherapy," says Tyler. "We've seen some incredible responses with some of these combinations in our preclinical animal test models, especially when we were systemically

The Stem Cell Hypothesis

James Grichnik, MD, PhD, associate professor of dermatology and director of the melanocytic diseases section in Duke's Division of Dermatology, explains a new hypothesis that melanoma springs from mutant stem cells. The model could help demystify the often strange behaviors of melanoma and offer more clues toward detection and treatment.

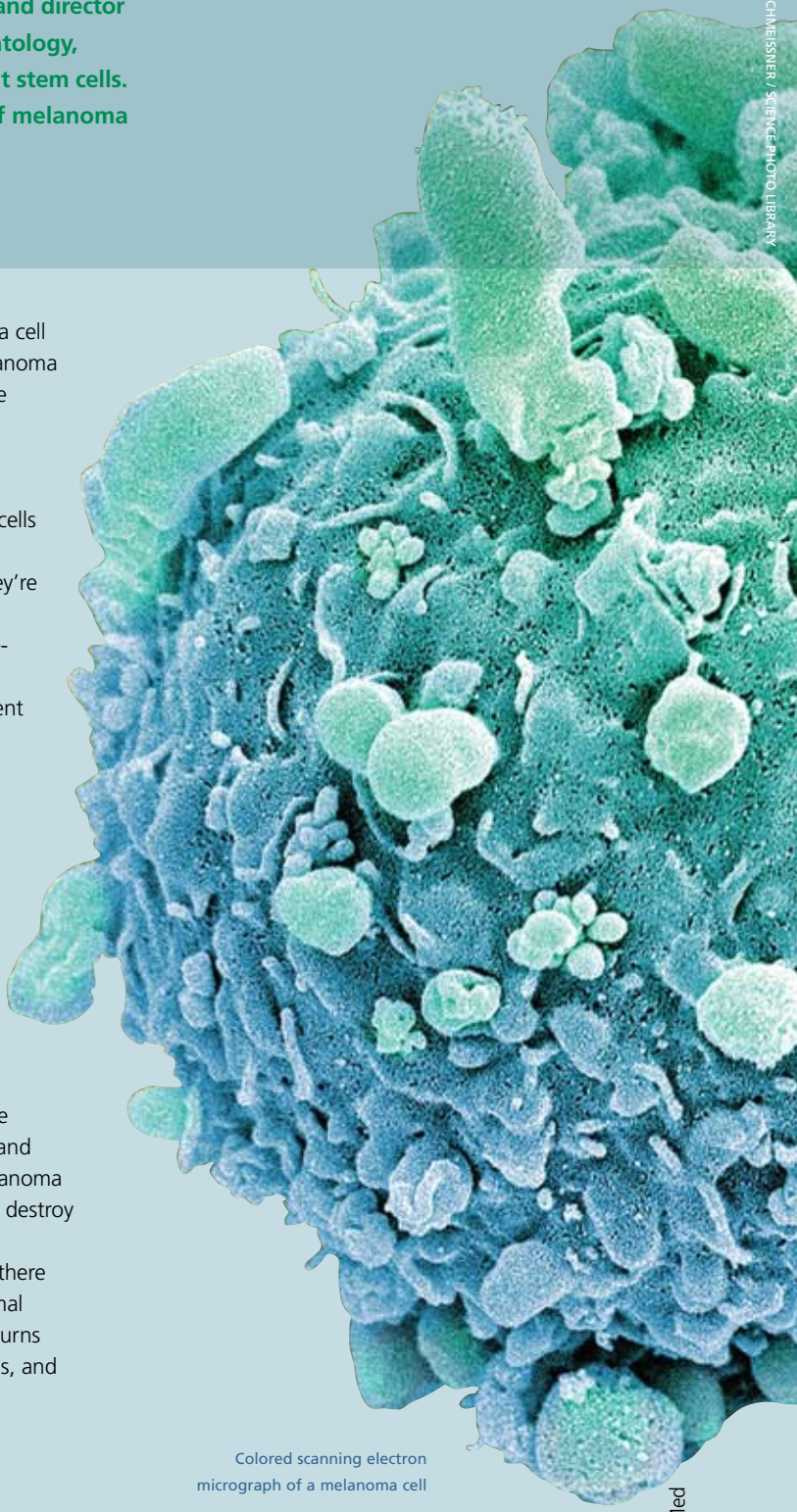
James Grichnik, MD, PhD

Our studies of metastatic melanoma cell lines support the hypothesis that melanoma develops from mutated stem cells. The idea is that there are stem cells sitting in the skin, and they accumulate mutations. When these stem cells are called upon to produce melanocytes (cells that produce pigment), if they have a benign complement of mutations, they're going to produce a benign mole. If they have a malignant complement of mutations, they're going to form a melanoma. This explains why three-fourths of melanomas develop directly from normal skin.

The mutated stem cell may also start growing with a benign complement of mutations but suffer an additional malignant mutation during that growth that results in the secondary development of a melanoma within a mole. This may explain the one-fourth of melanomas that develop in moles. What is also interesting is that through the use of dermoscopy (surface microscopy) we can identify specific growth patterns of different moles and melanoma types. We anticipate that someday we will be able to look at a lesion and, based on its growth pattern, be able to immediately predict what underlying pathways have been mutated and whether it is benign or malignant.

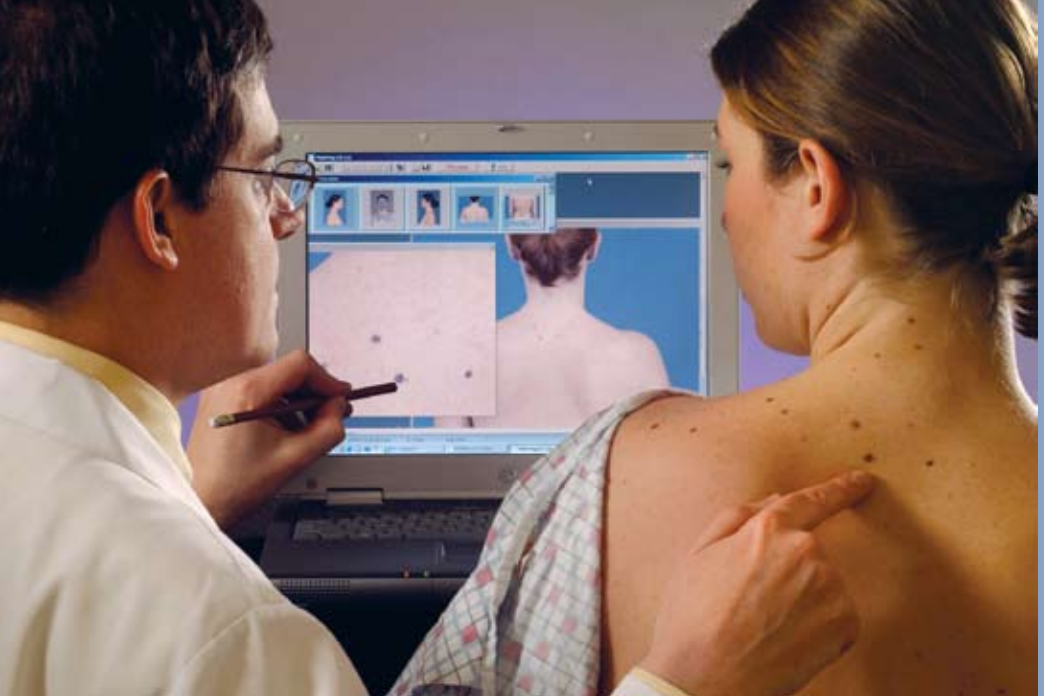
The stem cell model is consistent with the clinical phenomena that we're seeing. It could more easily explain behaviors like delayed onset and tumor dormancy. Cells could exist unstimulated for long periods in the body, and then when environmental conditions are appropriate, those mutated stem cells could again give rise to differentiating daughter cells and the tumor would become apparent. It might also explain death from melanoma despite a strong immunologic response. The immune system might easily destroy the malignant daughter cells but overlook the stem cells themselves.

We still have yet to conclusively prove the existence of these cells, but there are lots of papers being published now identifying different types of dermal stem cells, so I think it's just a matter of time. If the stem cell hypothesis turns out to be true, it will have major ramifications for the diagnosis, prognosis, and treatment of melanoma.



STEVE GSCHMEISSNER / SCIENCE PHOTO LIBRARY

Colored scanning electron micrograph of a melanoma cell



James Grichnik, MD, PhD, developed a CD-ROM-based medical record system that captures multiple images to create a standardized, comprehensive "map" of a patient's body. The total-body photography provides a baseline for mole comparison at future examinations.*

targeting a protein called N-cadherin. That protein is not expressed much in normal nevi [moles] or pigmented legions, but in melanoma, N-cadherin expression starts to increase, and it makes tumors much more invasive and aggressive."

The protein B-raf is also expressed abnormally in melanoma patients. The drug sorafenib, currently approved for renal cell cancers, targets B-raf. "There seems to be benefit in giving sorafenib systemically, then in the middle of this two-week systemic treatment giving regional therapy to the extremity," says Tyler. "We're interested in seeing what this drug may do for controlling metastatic melanoma."

Studies of these combination therapies in animals have been promising, and have led to phase-one clinical trials which are currently approved and open to patient accrual. "It's an exciting time," notes Tyler. "Hopefully things that we learn in this regional setting can then be extrapolated to help treat patients with more advanced systemic disease."

THE BIG PICTURE

While researchers are making headway with novel treatments for advanced melanoma, the best defense remains early detection of melanoma and prompt, thorough surgical intervention and follow-up.

"Our effort is to catch melanomas as early as possible," says James Grichnik, MD, PhD, director of the melanocytic diseases section in Duke's Division of Dermatology. "We can't identify a melanoma at the two-cell or four-cell or eight-cell stage; there is a threshold that these tumors need to cross before they can be identified. Thus, we all overlook early melanomas. Our effort is to help our patients and other physicians to identify melanomas as early as possible—well before the tumors have a chance to metastasize."

There's no advantage to removing every mole, says Grichnik. "There are roughly 200 thousand [benign] moles for every melanoma. Dysplastic nevi [atypical moles] cause a lot of anxiety among doctors and patients. There's this idea that it's just a matter of time before they turn into melanomas—this is nonsense. The large majority of dysplasic nevi will never turn into melanoma. About three-quarters of melanomas develop in normal skin. We need to think of dysplastic nevi as markers of patients who have increased risk of developing a melanoma. Don't use the terms 'precancerous' or 'premalignant' to describe dysplastic nevi—that really does a disservice by driving anxiety and unnecessary excisions."

For patients with extensive dysplastic nevi, especially in the setting of a personal or family history of melanoma, or those who have had melanoma and have a great deal of anxiety about reoccurrence, Grichnik uses total-body photography to provide a baseline for mole comparison at future examinations. Grichnik developed MoleMapCD, a CD-ROM-based medical record system that captures multiple images to create a standardized, comprehensive "map" of a patient's body.*

Change is one of the most important features of early melanoma, emphasizes Grichnik. "For patients with dysplastic nevi, the old ABCD criteria alone [suspecting melanoma based on a mole's asymmetry, border, color, and diameter] just falls apart." Recently E for "evolution" has been added to the criteria in an effort to boost its utility in melanoma detection.

Grichnik favors instead an approach termed "the smoking GUN of melanoma detection." GUN stands for **growth**, **unusual appearance**, and **non-uniform structure**. "In clinic this can be used efficiently by first looking for moles that don't match the others or are pointed out by the patient as concerning," he explains.

*MoleMapCD is a proprietary technology being marketed through DigitalDerm, Inc. for general use. Grichnik is a founder and major shareholder.

"Then by looking at the lesions very closely using dermoscopy [a type of surface microscopy] and determining whether they are uniform, showing the same pattern from the center to the edge in all directions. And then third, by checking the lesions against baseline photos for growth. Lesions that have grown and are unusual are already of some concern; if they are also non-uniform they are very worrisome for melanoma."

Surgeons typically don't encounter melanoma patients until after the diagnosis is made, but their ability to effectively treat the disease relies in part on the quality of the data collected before the referral. "Melanoma is a surgical disease, and you don't cut corners with it," says Samuel Fisher, MD, a pediatric otolaryngologist specializing in melanomas of the head and neck, which statistically are more aggressive and lethal than those elsewhere on the body. When diagnosing melanoma, he recommends a punch biopsy or an incision biopsy in the thickest area of the growth to determine its true depth. "A shave biopsy doesn't give you the full information."

"Pretty much everything else we do springs from knowing the depth of invasion," attests Pruitt, "such as whether we'd do a sentinel lymph node biopsy, a PET scan, a staging workup, and how widely we'd excise."

LIFE AFTER MELANOMA

Beyond treatment, ongoing vigilance is key for the melanoma survivor. "Once you have melanoma, your lifetime risk of having another one is five times greater," notes Fisher. "You need total body surveillance forever."

For Caddell, who has amassed a vast collection of hats, preaches the gospel of sunblock and tanning bed avoidance to whomever will listen, and endures an anxious day of CT scans every three months to confirm she's still cancer-free, life will never be the same, but she's finding her peace with that. "My prize is waking every morning and getting to still be here with my family."

While she credits Gollob and his team for saving her life, she's also grateful to the oncologist who sent her to Duke. "This disease is too fast, too furious—it's too big not to be in the hands of someone who can offer you all the options. At Duke, all the knowledge is under one roof. There's hope here." □

Learn more about clinical trials at Duke Comprehensive Cancer Center online: cancer.duke.edu/ctrials.

Melanoma in Minorities: Rarer but Deadlier

While melanoma is more common among Caucasians, with fair-skinned people with blond or red hair and blue, green, or gray eyes at even greater risk, melanoma affects people of all races. Though the melanoma incidence is lower among minorities, the five-year mortality rate from a melanoma is higher. "The heavier pigmentation helps reduce superficial spreading melanomas [the most common type] and lentigo-type melanomas [which typically occur on sun-damaged skin] but not acral lentiginous melanomas," says Grichnik. Acral lentiginous melanoma (ALM) represents a greater percentage of the melanomas among minority populations. ALM accounts for 50 percent of melanomas that arise in dark skin.

ALM is found on areas not commonly thought to be important sites for melanoma development, as they are not often sunburned: the palms and soles, beneath nails, and on mucous membranes. ALM in its early stages can look similar to a bruise or nail streak. "The differences in presentation can make these melanomas more difficult to recognize by the patient and physician and may delay diagnosis," warns Grichnik. As early detection is critical to survival, this underscores the need for greater awareness among patients and health care providers alike.

clinician Q+A

q: What are the latest approaches to managing high blood pressure?

a: Duke cardiologist Michael Blazing, MD, responds:

Despite all we know about the adverse health consequences of hypertension, it remains underdiagnosed and inadequately managed in the United States. Many of the estimated 65 million Americans with hypertension are not aware that they have the disease, and a significant portion of those who are known to have the problem do not have their blood pressure under adequate control. Yet improved diagnosis and control has the potential to yield huge benefits to society with regard to the prevention of cardiovascular disease, especially stroke.

What can be done to address this persistent problem? The obvious first step is to identify the millions of Americans who don't know they have elevated blood pressure. Screening programs sponsored by employers, senior centers, health departments, civic groups, and religious organizations are a great way to make people aware of their blood pressure reading and reinforce the importance of periodic evaluation for hypertension. The educational message should begin long before adulthood, however, and given the scope of the problem, the problem of hypertension should be a recurrent component of health education in our school systems.

Once identified, an affected individual must be encouraged to seek out a care provider to confirm the diagnosis—and an elevated blood pressure reading taken in the mall is often not enough impetus. The benefits of treating hypertension are well established, and especially the benefits with regard to long-term stroke risk reduction. Some of the reasons why people don't seek out medical attention include the absence of symptoms, a lack of knowledge about the seriousness of uncontrolled hypertension, a fear of potential side effects associated with treatment, and limited access to care. Some patients assume they will be faced with taking medications that they don't want to take or can't afford, and they don't want to be bothered with the inconvenience of regular office visits. Consider how many patients postpone seeing a physician even when they have alarming symptoms, like angina.

THE JNC 7 GUIDELINES

Once the diagnosis is confirmed, the health care provider is then faced with managing the condition. Here, there's guidance from the most recent report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), published in 2003.[1,2] The JNC 7 report offers a classification system that includes changing the term "high-normal" blood pressure to "prehypertension" because the committee felt the former term did not adequately alert patients to their risk of becoming hypertensive (Table 1). The report provides a treatment algorithm (Figure 2) that is also a component of a quick-reference office card that can be downloaded for free or purchased in a laminated form.[3]

The JNC 7 also listed seven key points for clinicians:

1. After age 50, systolic blood pressure > 140 is a much more important risk factor for cardiovascular disease (CVD) than elevated diastolic pressure.
2. Most older patients will become hypertensive; even people who are normotensive at age 55 have a 90 percent lifetime risk of developing hypertension, according to data from the Framingham study.[4]
3. Prehypertension begets hypertension, so think prevention. Lifestyle modification should be a part of treatment for all patients with hypertension or prehypertension.
4. Use thiazide diuretics, either alone or in combination with drugs from other classes, unless there are compelling reasons to do otherwise (such as renal disease and recent myocardial infarction). The results of ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial), the largest hypertension trial of its kind with more than 42,000 participants aged 55 and older, provided strong scientific evidence for this recommendation.[5]
5. Most patients will require two or more drugs to achieve goal blood pressure.
6. For patients with higher blood pressure (>20 mmHg systolic or 10 mmHg diastolic above goal pressure), start therapy with two agents, including a thiazide diuretic.
7. Work with the patient to build adherence. Build empathy, trust, and motivation by making sure the patient understands and agrees with the goals of therapy (by providing current and goal blood pressure readings verbally and in writing) and removing barriers to care whenever possible (such as the cost of medications and the complexity of care).

Another key point worth adding to the list is to treat the disease aggressively when the blood pressure readings indicate that medication is needed. The old adage "start

BLOOD PRESSURE CLASSIFICATION

Category	Systolic Blood Pressure (mmHg)		Diastolic Blood Pressure (mmHg)
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Stage 1 hypertension	140-159	or	90-99
Stage 2 hypertension	≥160	or	≥100

Table 1. Table 1 and Figure 2 courtesy National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services.

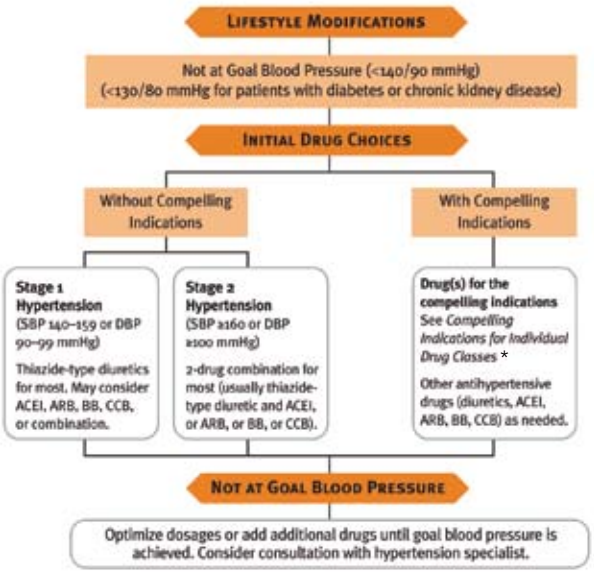


Figure 2: ALGORITHM FOR TREATMENT OF HYPERTENSION.
*For more information, including strategies for improving adherence to therapy and a list of compelling indications for individual drug classes (referenced above), visit www.nhlbi.nih.gov/guidelines/hypertension/jnc7card.htm.

low and go slow" no longer seems prudent. The former prescribing pattern of sequential monotherapies—trying one drug, then switching to a different drug when the first one doesn't lower the blood pressure to goal—has lost favor to the additive strategy (and, as noted in #5 above, patients are likely to need more than one drug). Although the vast majority of patients have essential hypertension, it's likely that they have several pathophysiologic mechanisms contributing to their disease and will benefit from a combination strategy that addresses these mechanisms. This move to combination therapy requires clinicians to be aware that certain populations such as the elderly and patients with diabetes or autonomic dysfunction will require additional instruction and monitoring to minimize potential side effects of the medications.

THE BETA-BLOCKER CONTROVERSY

The decision to convene the JNC 7 committee in 2003 to update the guidelines was based in part on the publication of many new hypertension observational studies and clinical trials since the release of the previous guidelines in 1997. One important study not available in 2003 is the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT). The results from this long-term study of 19,000 European patients with hypertension were not available until late 2004 and have some experts in this country calling for updates to the current guidelines.[6] ASCOT, which compared the combination of a calcium channel blocker (CCB) and an angiotensin-converting enzyme (ACE) inhibitor to a beta-blocker and thiazide diuretic, was halted in December 2004 when an interim analysis found better outcomes for a wide range of cardiovascular events among patients receiving the CCB-ACE inhibitor combination. Concerns about the use of beta-blockers as first-line treatments had been building for nearly a decade, and now meta-analyses of the use of beta-blockers in uncomplicated hypertension support the findings of ASCOT.[7,8]

In June 2006 the United Kingdom's National Institute for Health and Clinical Excellence (NICE) and the British Hypertension Society issued updated guidelines that relegate beta-blockers to a third- or fourth-line drug.[9] The guidelines also note that there is not an urgency to stop beta-blockers (particularly in someone whose blood pressure is well controlled) and that doing so abruptly can cause harm. Moreover, patients with a compelling reason to take beta-blockers, such as angina or a previous MI, should certainly continue on the drug.

continued

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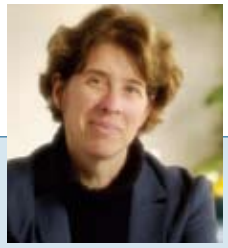
ADHERENCE

Finally, health care professionals constantly deal with the issue of patient adherence—and it's especially difficult with a silent disease like hypertension. Patients who come in symptom-free but need medications start having side effects, like frequent urination, and don't want to continue with the drugs. Or the medication regimen is too complicated, or too costly. Or the patents aren't motivated to make any lifestyle changes.

As noted in the JNC 7 guidelines, we need to work with our patients to maintain adherence. We can build empathy, trust, and motivation by making sure the patient understands and agrees with the goals of therapy—by providing current and goal blood pressure readings verbally and in writing, for instance. We must make sure they understand that hypertension is a chronic disease that won't simply go away without some effort on their part to modify lifestyle factors that contribute to the problem and consistently to take medications that are returning their system toward their desired baseline values. And we should try to remove barriers to care whenever possible, choosing less expensive alternative medications and less complex dosage schedules. We hope that our efforts to manage this huge and costly medical problem will help reduce the morbidity and mortality caused by this silent disease.

Michael Blazing, MD, is director of the Adult Inpatient Cardiology Service at Duke University Hospital.

clinician Q+A



q: What are the most effective lifestyle modifications for managing hypertension?

a: Duke hypertension specialist Laura Svetkey, MD, responds:

With so many different and effective medications available that can lower blood pressure, it's easy to understand why discussions about hypertension seem to revolve around the latest drug studies. But we need to remember that lifestyle changes can have a significant beneficial impact on blood pressure as well as on the cardiovascular and overall health of our patients.

THE BIG FIVE

The Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommends five nonpharmacologic lifestyle modifications: achieving a healthy weight, limiting sodium intake, increasing exercise, moderating alcohol consumption, and adopting the DASH (Dietary Approaches to Stop Hypertension) eating plan. The first four are well-known health recommendations, but patients may not be familiar with DASH. The first DASH clinical trial, sponsored in the 1990s by the National Heart, Lung, and Blood Institute, demonstrated the beneficial effect of an eating plan that combines specific micro- and macronutrients associated with lowering of blood pressure—potassium, calcium, magnesium, and fiber.[1,2] The DASH eating plan outlines a diet rich in fruits and vegetables, high in low-fat dairy products, and low in total and saturated fats. The standard DASH plan is based on consuming 2,000 calories a day, but the plan can be easily adapted for lower calories as a weight-loss strategy (and the high-fiber nature of the plan helps curb hunger).

DASH is also not strictly a low-salt plan since it is effective at lowering blood pressure at typical American levels of salt consumption. However, it is more effective if combined with the current government dietary guidelines of no more than 2,400 mg of sodium a day.[3,4] Further lowering salt intake makes DASH even more effective, but this is not possible without eating special foods and is therefore not practical for most patients. The bigger blood pressure effect comes from DASH, with a small additional increment from lowering sodium intake, so our emphasis should be on adopting DASH.

Reducing sodium intake can be especially difficult for our patients because about 85 percent of the sodium consumed in a typical American diet is already in the food and not added at the table or in cooking. Canned and processed foods are especially high in sodium, as are most fast-food items. In fact, about the only real salt-free zone in the grocery store is the fresh produce section, and the emphasis on these foods in the DASH plan certainly

helps its followers keep sodium consumption within the suggested range.

Limiting alcohol consumption is another important lifestyle modification, as there is a dose-response relationship between decreased alcohol consumption and blood pressure reduction.[5] Furthermore, drinking outside of meals appears to have a significant effect on hypertension risk independent of the amount of alcohol consumed.[6] JNC 7 recommends that men limit alcohol consumption to no more than two drinks per day and women to no more than one per day.

WEIGHTY EVIDENCE

Of the five lifestyle modifications, weight loss has the greatest beneficial impact on hypertension (not to mention lowering the risk of developing diabetes and improving lipid profile). A recent analysis from the Framingham study found that even modest amounts of weight loss can substantially reduce the risk of hypertension over time—a loss of 15 pounds or more was associated with 21 to 29 percent reduction.[7] In addition to preventing hypertension, weight loss clearly lowers blood pressure in those with hypertension and prehypertension. Meta-analyses estimate that 10 pounds of weight loss leads to systolic blood pressure reduction of five to 10 mmHg.[8] We are all well aware of the obesity epidemic in this country and its relationship to a variety of health problems, and health care providers should do whatever possible to help our patients lose excess weight and maintain the loss.

Aerobic exercise goes hand-in-hand with weight loss, has beneficial effects on blood pressure whether or not the person has hypertension, and improves cardiovascular health. Current JNC 7 recommendations suggest that patients with prehypertension or hypertension participate in at least 30 minutes of moderate aerobic activity, such as a brisk walk at lunch, at least four times a week.

LIFESTYLES AND REAL LIFE

Although two DASH trials demonstrated that diet can lower blood pressure, they were conducted in a highly controlled fashion, with all meals prepared in a research kitchen and provided to each participant for the duration of the studies. The subsequent PREMIER trial looked at whether individuals could institute several lifestyle changes at the same time if assisted by behavioral intervention. An advice-only control group got printed materials and a 30-minute session with a nutritionist that included minimal counseling on making behavioral changes. The "established" group received 20 weekly counseling sessions about lifestyle modification and kept track of their calorie and sodium intake and exercise. The "established plus DASH" group were also taught to follow the DASH diet and record their servings of fruits, vegetables, dairy products, and fat.[9]

Both the established lifestyle modification group and the established plus DASH group lost weight, reduced their sodium intake, increased their physical fitness, and improved their hypertension status (an average decrease of 10.5 mmHg systolic and 6.4 diastolic), and those following the DASH plan improved to a comparable extent (11.1 systolic and 5.5 diastolic). The established plus DASH group also made healthy improvements in diet such as increased intake of fruits, vegetables, and low-fat dairy, and decreased intake of fat. These lifestyle changes were largely sustained over 18 months, even though they received only monthly counseling after the first six months.[10]

Interestingly, however, the advice-only group also experienced improvements in blood pressure, although not to the same extent as the other groups (6.6 systolic and 3.8 diastolic); and they lost a little weight (three pounds vs. 13 pounds for established plus DASH and 11 pounds for established intervention). Even though the randomly assigned advice-only group was not counseled on a weekly basis, we can assume they were highly motivated individuals because they were willing to enter this clinical trial and undergo the required extensive screening process. We should never underestimate the role patient motivation plays in the success of any treatment we prescribe.

The PREMIER trial demonstrates that lifestyle changes alone can improve the hypertension status of our patients. Moreover, it points out the significant effect that advice from a health care professional can have on patients. In the current health care climate, we often feel like we do not have sufficient time to spend counseling patients. But we must remember that reinforcing the healthy-lifestyle message verbally and with written materials has a real and positive effect on our patients. Considering the cost of treating more than 65 million Americans with antihypertensive drugs, can we afford not to emphasize these low-cost, side-effect-free alternatives to our patients?

Laura Svetkey, MD, is director of the Duke Hypertension Center and director of clinical research at the Sarah W. Stedman Nutrition and Metabolism Center at Duke.

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Gifts from individuals and organizations are the largest source of non-government support for Duke's research, education, patient care, and service missions. Here are some recent examples of philanthropic partnerships that will make a difference to human health for generations to come. **To learn more about how you can support medical education, research, and patient care at Duke, please call 919-667-2500 or visit development.mc.duke.edu.**

Chance and friendship combine to launch Anesthesia DREAM Campaign

Five years ago Peter Waweru was a farmer and high-school English and biology teacher in Kenya. Today he is a clinical trials specialist in Duke's Clinical Anesthesiology Research Endeavors (CARE) Program. Chance played a major role in getting Waweru where he is today, but people-to-people connections helped him contribute to his new community in a powerful way.

The chain of events started when Waweru, 43, and his wife, Gladwell, won the U.S. State Department-sponsored Diversity Visa lottery and received permanent-resident status in the U.S. The lottery didn't include housing or employment, but the Wawerus planned their move nonetheless and the couple arrived in Durham in 2002 with their two young sons. Peter began taking night classes toward an associate's degree in clinical research while working a day job at the seafood counter of a local grocery store.

That's where he met the wife of Joseph P. Mathew, MD, division chief of cardiothoracic anesthesiology at Duke and medical director of CARE. Over a series of seafood purchases, Mrs. Mathew and Waweru became friends; on his wife's recommendation, Mathew invited Waweru to interview for a research position, and later hired him.

ELIZABETH T. PEREZ

Peter Waweru (left), a recent immigrant from Kenya, connected community entrepreneur Bud Doughton (right) with Duke's Anesthesiology Department to help launch a fundraising campaign for research to improve outcomes after surgery and anesthesia.

In the meantime, Waweru and his family had found a place to live through St. Mark's Anglican Church, which once held services in an old church building on the property of the former Methodist Retirement Home. A local developer, Anthony & Co., is now redeveloping the Erwin Road property as Lakeview, but until the construction started, the church and the developer decided to sponsor housing on the property for numerous immigrant families like the Wawerus.

An attorney for Anthony & Co. and church member, Jack Markham, introduced Peter Waweru to Bud Doughton, one of the investor-owners and a developer of Lakeview.

"Jack brought Peter to us at the perfect time, since we needed someone on the property to handle security, property management, and groundskeeping," says Doughton.

He and Waweru forged an immediate friendship. "My wife and I will forever be grateful to Bud for his generosity and kindness," says Waweru. "He is also a good friend and mentor to my two sons, Wilson and Kelvin."

As Waweru became more involved with his work at Duke, he learned about the Department of Anesthesiology's plans to launch a fundraising drive, the Duke DREAM (Developing Research Excellence in Anesthesia Management) Campaign. The campaign will support anesthesia management research, particularly developing methods to protect the brain and other organs during surgery and general anesthesia.

Waweru introduced the DREAM campaign director, Elizabeth Perez, to Doughton. Soon, Anthony & Co. signed on as the founding sponsor with an initial gift of $100,000 to the DREAM campaign.

"It has been our goal since the day we acquired the [Erwin Road] property to find ways to serve the community," says Catherine Miller, president of Anthony & Co.

Waweru's initiative and Anthony & Co.'s support will lead to the official Duke DREAM campaign kickoff later in 2007, completing a full circle of community partnership at the personal, academic, and business levels.

"Anthony & Co. is about transforming communities, and that translates to people's lives," said Jim Anthony, CEO and founder. "We are thrilled to be part of the DREAM to assist with the transformational mission of improving patients' quality of life after anesthesia and surgery."

For more information, visit dreamcampaign.duhs.duke.edu.

Community rallies for Duke Children's

People and organizations across North Carolina dialed in to help raise $1,004,591—a new record—during the 13th Annual Radiothon for Duke Children's Hospital & Health Center on MIX 101.5 and 99.9 Genuine Country in February. The Radiothon is one of the most successful and longest running events of its kind.

Bassett Professorship honors former Duke team doctor

A few months before his death in March, professor emeritus of orthopedic surgery Frank Bassett, MD, learned that his friends and colleagues had contributed nearly $1 million to establish the Frank Bassett, MD, Assistant Professorship in Orthopedics. Bassett served as head team physician for Duke Athletics for 30 years. He also contributed to the professorship with a planned gift from his estate.

The lead gift, a $400,000 planned estate gift, came from Doris, N'48, and Richard N. Wrenn, T'43, MD'47, HS'47-'54, of Charlotte, North Carolina. Dr. Wrenn is a retired orthopedic surgeon who trained at Duke. The completion of the professorship was announced at a December gathering honoring Bassett's contributions to medicine. Bassett taught some 350 orthopedic residents and fellows during his time at Duke, including a cohort of fellows from the University of Ioannina, Greece—one of whom, Panayotis N. Soucacos, MD, HS'74, attended the gathering.

Mandel gift funds hypertension and atherosclerosis research

Pictured from left are Chancellor Dzau; Mandel Foundation trustees Edwin Ruthman, Henry Lawrie Jr., and Judith Pieper; and Thomas Coffman, MD.

A commitment of over $2 million from the Edna and Fred L. Mandel Jr. Foundation will support Duke research on the causes and treatment of atherosclerosis and hypertension, as well as collaboration among scientists at Duke and other medical centers.

An initial $750,000 grant has established the Mandel Center for Hypertension and Atherosclerosis at Duke and is renewable for an additional two years. Senior Investigator Awards went to Victor J. Dzau, MD, James B. Duke Professor of Medicine and chancellor for health affairs; Thomas Coffman, MD, chief of nephrology; Laura Schanberg, MD, associate professor of pediatrics in rheumatology; and the team of Michelle Winn, MD, assistant professor of medicine in nephrology, and Paul Rosenberg, MD, assistant professor of medicine in cardiology. A separate Young Investigator Award went to Thomas Povsic, MD, assistant professor of medicine in cardiology, to study the cells that repair damage in atherosclerosis and their possible use in predicting heart attack and stroke risk.

To increase scientific collaboration among scientists at Duke and other research institutions, the Mandel Center will offer monthly seminars at Duke beginning in May 2007, and later an off-campus scientific retreat.

New fellowship honors Wilfert

Duke pediatric HIV/AIDS researcher and children's global health advocate Catherine Wilfert, MD, was honored in March with the establishment of an endowed fellowship in pediatric infectious diseases in her name. Wilfert, a Duke professor emerita of pediatrics and microbiology, is internationally known for her research into the natural history and treatment of AIDS in children and her involvement in clinical trials to test the effectiveness of new anti-HIV medications, particularly the use of AZT to block transmission of the AIDS virus from mother to baby. Friends and colleagues of Wilfert and her husband, Samuel Katz, MD, chair emeritus of pediatrics, contributed more than $850,000 toward the endowment fund.

Golfers unite against melanoma

Melanoma cut short the career of former professional golfer Michael Muehr, T'94, and now he's enlisted the help of fellow golfers to beat the disease. Muehr and the organization he leads, Golf Pros Beating Cancer, have given $175,000 in proceeds from the first and second annual Capital City Pro Am, held in the Washington, D.C. area, to fund a melanoma clinical trial at Duke.

The clinical trial, led by Doug Tyler, MD, professor of surgery, and Scott Pruitt, MD, associate professor of surgery, with Hilliard Siegler, MD, professor of surgery, as advisor, will test a potential immunotherapy vaccine.

"I enjoy an overwhelming feeling of gratification when it comes to raising money for melanoma research," says Muehr, who played on the PGA Tour and in the U.S. Open during his nine-year career. "The response I have received from all those who support our events has elevated this effort well beyond my own expectations and dreams."

Proceeds from the third annual Capital City Pro Am, September 9-10, 2007, at Lowes Island Club in Potomac Falls, Virginia, will also fund melanoma research at Duke.

New leadership structure for School of Medicine

In a move to position Duke Medicine for continued growth and academic success, **R. Sanders Williams, MD**, the current dean of the Duke University School of Medicine, has been appointed to the newly created position of senior vice chancellor for academic affairs.

Williams will continue to serve as dean of the medical school until a new dean has been identified through a search process now under way. Williams will also retain his title as dean of the Duke/National University of Singapore Graduate Medical School (GMS) through the completion of the 2007-08 academic year. Both the new dean of the Duke School of Medicine and the new dean of the GMS will report directly to Williams.

In his new role, Williams will have primary responsibility for academic success across the entities that comprise Duke Medicine, enhancing collaboration between the Duke University School of Medicine and the GMS in Singapore. He will also lead the implementation of the strategic plans for the schools of medicine, working closely with the medical school deans as a team, and lead the Duke University School of Medicine's philanthropic and fundraising efforts. Williams will report directly to Victor J. Dzau, MD, chancellor for health affairs at Duke and president and CEO of the Duke University Health System.

"The scale and complexity of the academic, research, and clinical care missions of the school have quickly grown to a point that they now demand a greater breadth and intensity of high-level leadership," Dzau says. "This new leadership framework will facilitate greater strategic effectiveness for the School of Medicine and will distribute leadership responsibilities, allowing a higher degree of focus by the deans and the senior vice chancellor."

Over the past six years under Williams's leadership, Duke's School of Medicine has experienced significant growth, including an annual budget that now exceeds $800 million, a near doubling of research funding from the National Institutes of Health to almost $350 million, the construction of five new research buildings, the creation of the GMS in Singapore, the development of several new national and international research institutes, and an increase of several hundred new faculty.

"I am excited about the opportunities presented by this new role and believe strongly that the addition of a new senior leader in the role of dean of the Duke University School of Medicine will greatly increase our strategic effectiveness," Williams says.

McKinney to direct Trent Center

After five years as vice dean for research with the Duke University School of Medicine, **Ross McKinney, MD**, has accepted the role of director of the Trent Center for Bioethics, Humanities, and History of Medicine.

In his new role, McKinney will report to the dean of the medical school, and will continue to provide administrative leadership and oversight to the Conflict of Interest committee. In addition, McKinney will continue to be a major contributor to the new Duke Translational Medicine Institute initiative.

Executive vice dean for GMS Singapore

Ranga Krishnan, MD, has been appointed executive vice dean for the Duke-National University Singapore Graduate Medical School (GMS), effective July 1, 2007. In this role, Krishnan will work closely with R. Sanders Williams, MD, senior vice chancellor for academic affairs and GMS dean, with full administrative, operational, and educational decision-making authority for the GMS subject to Williams's oversight as dean.

Krishnan will continue to serve concomitantly as chair of Duke's Department of Psychiatry, working with a team of three vice chairs—**Marvin Swartz, MD**, clinical affairs, **Richard Surwit, PhD**, research, and **Dan Blazer, MD, PhD**, education—to continue to provide the exemplary leadership that has been characteristic of his tenure as chair, Williams said in announcing the appointment.

"Dr. Krishnan's deep familiarity with the region and GMS, as well as his track record of successful leadership, made him an ideal choice to take on this responsibility," Williams said. "I am confident that he is fully capable of succeeding in both of these important roles."

Cohen named chair of medicine

Harvey Jay Cohen, MD, has been named chair of Duke's Department of Medicine by R. Sanders Williams, MD, senior vice chancellor for academic affairs. The appointment in March follows Cohen's service as the department's interim chair beginning February 2006.

"Harvey brings the right combination of achievement, leadership experience, communication skills, and sound judgment to this important position," Williams says. "During his period of interim service, he has earned the respect of faculty and senior leadership of Duke Medicine alike."

Cohen previously served as the Department of Medicine's vice chair for faculty development and academic affairs. He helped to establish Duke's Division of Geriatric Medicine in the 1970s and served as division chief until becoming chair of medicine. He was also the architect of Duke's fellowship program in geriatric medicine. He is a professor of medicine and director of Duke's Center for the Study of Aging and Human Development.

"I have been at Duke for many years and have worn several hats in my career. I am honored to be able to continue serving Duke in this position of such great tradition and importance," says Cohen.

Duke's program in internal medicine has been consistently recognized as one of the best in the nation in National Institutes of Health funding. Under Cohen's leadership, Duke's program in geriatric medicine was ranked fourth in the nation in the *U.S.News & World Report* 2006 rankings.

New leaders in cardiovascular medicine

Duke's Department of Medicine in May announced the formation of a new leadership team for the Division of Cardiovascular Medicine. **Howard Rockman, MD**, was named division chief, and **Chris O'Connor, MD**, was named director of the Duke Heart Center.

Rockman

O'Connor

"Dr. Rockman is an outstanding clinician and basic scientist who has done groundbreaking work to enhance our understanding of the molecular pathogenesis of heart failure," said Harvey Cohen, MD, chair of medicine, in announcing the appointments. "Dr. O'Connor is a highly regarded clinician and clinical researcher who has played a leading role in the development of our heart failure service and patient-oriented research in cardiology. I am confident that this team can work with our faculty to enhance our academic success, while forging effective and productive relationships with the Health System."

Rockman succeeds Pamela Douglas, MD, who is stepping down to join the Duke Clinical Research Institute (DCRI). As division chief, Douglas ably represented Duke on the international scene as president of the American College of Cardiology, and oversaw an outstanding group of faculty and fellows, said Cohen.

Also in May, Rockman named Thomas Bashore, MD, as division vice chief; Bashore will play a vital role in cardiovascular medicine education and clinical programs.

Network Services appointments

Duke cardiologist **Harry Phillips III, MD**, has been appointed as chief medical officer of Duke University Health System (DUHS) Network Services. In this role, Phillips will work closely with both affiliate communities and clinical leadership at Duke to strengthen clinical care delivery across the region. In addition, **Paul Lindia** was named associate vice president of Network Services, succeeding Malcolm Isley, who will join Greenville Hospital System in South Carolina. The appointments were announced in May by Molly K. O'Neill, DUHS chief strategic planning officer.

Phillips

Benfey to lead new systems biology center

The Duke Institute for Genome Sciences & Policy (IGSP) in March announced the establishment of the IGSP Center for Systems Biology.

Philip Benfey, PhD, Paul Kramer Professor and current chair of the Department of Biology, has been appointed director of the center. Benfey will step down as department chair effective June 30.

Systems biology is a relatively new field that uses the massive amounts of data produced by automated and computerized laboratory equipment to look for large patterns and networks among the molecular components of individual cells. The IGSP Center for Systems Biology has the primary goal of nurturing interactions between experimental scientists and theorists with a common interest in biological systems.

Benfey

"Under Philip's leadership, the new center will build on the growing use of genome-level data to describe and understand the complex interactions among the full set of gene products in cells of many organisms, from yeast to plants to mammals," says IGSP Director Huntington Willard, PhD. "This new center nicely complements the other IGSP centers and further strengthens our interdisciplinary ties across campus."

Pictured are five of the six Duke Med Scholars: (from left) Terry Lechler, PhD, Michelle P. Winn, MD, Farshid Guilak, PhD, Rob Wechsler-Reya, PhD, and Tannishtha Reya, PhD. Not pictured: Paul Noble, MD.

Investing in the future of science

In February the School of Medicine announced its inaugural six Duke Med Scholars. The new program was conceived as part of the School of Medicine's strategic plan, which focuses on people, places, and programs. The awards provide additional financial support to faculty members who appear poised to make the next big step forward in their research and their careers.

The first group of Scholars includes:

- **Farshid Guilak, PhD**, Laszlo Ormandy Professor of Orthopedic Surgery and professor of biomedical engineering. From growing cartilage from fat cells to creating a fabric "scaffold" that can assist in repairing damaged joints, Guilak's research blends biomedical engineering and a keen interest in functional orthopedic surgery. Guilak is also studying ways to slow cartilage breakdown caused by osteoarthritis.

- **Terry Lechler, PhD**, assistant professor of cell biology, who studies the morphogenesis of epithelial cells. Lechler's research has shown that skin cells can divide either symmetrically or asymmetrically and that asymmetric divisions promote formation of multiple cell layers to form a protective barrier. Lechler is also investigating how a cell's function depends on its shape and what happens when the shape goes awry.

- **Paul Noble, MD**, professor of medicine and chief of pulmonary medicine, whose research focuses on understanding the mechanisms that regulate chronic lung inflammation and fibrosis. In particular, he has focused on the role of the extra-cellular matrix in regulating chronic lung inflammation.

- **Tannishtha Reya, PhD**, assistant professor of pharmacology and cancer biology, who studies hematopoietic stem cells. Her investigations could shed light on the signals that control development of the hematopoietic system and its effects in cancer. Understanding the normal regulation of stem cell renewal may allow the development of approaches to enhance regeneration and thus have implications for therapies.

- **Rob Wechsler-Reya, PhD**, assistant professor of pharmacology and cancer biology, whose research centers on the development of the cerebellum and the genesis of medulloblastoma, the most common malignant brain tumor in children. His research has shed light on the tumor's early stages and identified genes important for tumor formation. Ongoing studies are aimed at developing new models for medulloblastoma and identifying more effective treatment strategies.

- **Michelle P. Winn, MD**, assistant professor in nephrology and the Center for Human Genetics, whose current research interest is familial focal and segmental glomerulosclerosis (FSGS), a kidney disorder. Although most people affected by FSGS do not have a family history of kidney disease, Winn hopes to increase prevention and treatment for the more common sporadic disease, which affects up to 20 percent of patients on dialysis.

Lefkowitz receives America's top prize in medicine

On April 26, **Robert J. Lefkowitz, MD**, added another trophy to the extensive honors he has collected over his 35-year career, sharing one-third of the $500,000 Albany Medical Center Prize in Medicine and Biomedical Research—America's top prize in medicine.

He was recognized for a lifetime of work that inspired a new generation of safer and more effective prescription drugs for a wide variety of ailments, including coronary heart disease, schizophrenia, breast and ovarian cancer, atherosclerosis, asthma, arthritis, and diabetes. The key to all of this was his research leading to understanding of elusive chemical receptors on the surface of cells. These receptors have become the target of beta blockers, cortisone, antihistamines, antidepressants, estrogens, androgens, contraceptives, insulin sensitizers, and obesity pills.

"Bob's one of the great scientists of the century, and he's not through yet," says R. Sanders Williams, MD, dean of the Duke University School of Medicine and senior vice chancellor for academic affairs, and a protégé of Lefkowitz's.

Lefkowitz, the James B. Duke Professor of Medicine and Howard Hughes Medical Institute investigator, shared the prize with Solomon Snyder, MD, of Johns Hopkins School of Medicine, and Ronald Evans, PhD, of The Salk Institute for Biological Studies.

They will each receive one-third of the Albany Prize's $500,000 award for their pioneering work on how cells receive signals from their surrounding environment, an essential function that mediates the "fight or flight" response and most sensory inputs like sight, taste, and smell.

This article is excerpted from a profile of Lefkowitz published in INSIDE Duke Medicine. *To read the full article visit dukemedmag.duke.edu.*


Darell Bigner, MD, PhD


Pamela Edwards, EdD, RN


Larry B. Goldstein, MD


Robert Jennings, MD

Darell Bigner, MD, PhD, was recently awarded the Tug McGraw Researcher of the Year Award from the Tug McGraw Foundation for his outstanding leadership in the field of brain tumor research.

Bigner is the Edwin L. Jones Jr. and Lucille Finch Jones Cancer Research Professor and the director of the Preston Robert Tisch Brain Tumor Center at Duke. The Tug McGraw Foundation, named in memory of the baseball legend, raises funds to support brain cancer research and seeks to increase awareness of the disease. In 2004 a grant from the foundation supported the creation of the Tug McGraw Center for Neuro-Oncology Quality of Life Research at Duke.

Pamela Edwards, EdD, RN, received the 2006 Juanita Long Award of the Beta Epsilon (Duke School of Nursing) chapter of Sigma Theta Tau in December. Edwards is an associate consulting professor and director of the Nursing Education Program at the Duke University School of Nursing, serves as deputy director of the Duke AHEC program, and is the associate chief nursing officer for education at DUHS.

Since 2004, Sigma Theta Tau has presented the Juanita Long Award each year to an outstanding nurse whose contributions to nursing fulfill the goals of Sigma Theta Tau and exemplify nursing leadership qualities.

Michael Ehlers, MD, PhD, associate professor and Wakeman Scholar in the Department of Neurobiology and Howard Hughes Medical Institute investigator, received the 2007 John J. Abel Award. The award, sponsored by Eli Lilly & Co., is given to a single young investigator for outstanding research contributions in pharmacology. Ehlers's research focuses on brain plasticity and specifically on the cell biological basis of neural plasticity. He received the award April 28 at the annual meeting of the American Society for Pharmacology and Experimental Therapeutics/Experimental Biology.

The Hartwell Foundation has selected two Duke researchers to receive its inaugural Hartwell Individual Biomedical Research Awards for 2006.

The awards provide support to individual researchers at eligible research facilities across the country for three years at $100,000 per year. Duke was one of nine qualifying institutions and one of three to receive two individual research awards. Each participating institution also received funding for a postdoctoral candidate of its choice to receive the Hartwell fellowship.

The Duke research award winners are: **Guopeng Feng, PhD**, of the Department of Neurobiology, for his work to identify the genes involved in obsessive-compulsive disorder; and **Jingdong Tian, PhD**, of the Department of Biomedical Engineering, Pratt School of Engineering, and the Institute for Genome Sciences & Policy, for new technologies and methods to develop optimized quick-response DNA vaccines for infectious diseases.

Nancie Jo MacIver, MD, PhD, an endocrinologist in the Department of Pediatrics, was selected to receive the fellowship for her work on the hormone leptin, which may help prevent infection in children with suppressed immune systems caused by malnutrition in infancy or in utero.

Larry B. Goldstein, MD, professor of medicine in neurology, has received the American Heart Association (AHA) 2007 Award of Meritorious Achievement for his work on stroke-related initiatives. Goldstein, director of the Duke Center for Cerebrovascular Disease and the Duke Stroke Center, also chairs AHA's Stroke Council, a body charged with developing scientific policy and advancing the science of stroke care. He is the immediate past chair of the American Stroke Association and president-elect of the AHA Mid-Atlantic Affiliate.

Robert Jennings, MD, James B. Duke Professor of Pathology, has received the 2007 Gold-Headed Cane Award, the highest honor of the American Society of Investigative Pathology (ASIP), which recognizes long-term contributions to pathology.

Jennings's contributions in renal disease and cardiovascular research span over 50 years. "He is the 'founding father' of modern ischemic biology," said Roberto Bolli, MD, of the University of Louisville Health Science Center. "More than anyone else, Dr. Jennings must be credited with crafting the conceptual, pathophysiological, and preclinical framework that enabled the development of thrombolysis, percutaneous coronary angioplasty, and other forms of therapeutic recanalization in patients with acute myocardial infarction—one of the most spectacular triumphs of modern clinical cardiology."

Jennings received the Gold-Headed Cane, a mahogany cane topped with a 14-karat-gold head and engraved band, at the ASIP annual meeting on April 29.

Pictured from left are the medical school's 2007 faculty award winners: L. Scott Levin, MD, John D. York, PhD, Robert P. Drucker, MD, William St. Clair, MD, Emma (Mimi) Jakoi, PhD, and Mohamed Noor, PhD. Not pictured: Neil Prose, MD.

The following awards were presented at the annual School of Medicine faculty meeting in May:

- Leonard Tow Humanism in Medicine Award: **Neil Prose, MD**, professor of medicine and pediatrics
- Leonard Palumbo Jr., MD, Faculty Achievement Award: **Robert P. Drucker, MD**, associate professor of pediatrics
- Ruth and A. Morris Williams Jr. Faculty Research Prize: **John D. York, PhD**, associate professor of pharmacology & cancer biology and of biochemistry
- Gordon G. Hammes Faculty Teaching Award: **Mohamed Noor, PhD**, associate professor of biology
- Master Clinician/Teacher Awards: **L. Scott Levin, MD**, professor of surgery and chief of plastic and reconstructive surgery; **William St. Clair, MD**, professor of medicine and immunology; **Emma (Mimi) Jakoi, PhD**, associate research professor of cell biology.

Vance Fowler, MD, and **Eric Peterson, MD**, of the Duke Clinical Research Institute and **Jeremy Rich, MD**, of the Division of Neurology were recently elected to the American Society for Clinical Investigation, an honor society of physician-scientists who translate findings in the laboratory to the advancement of clinical practice. The society elects up to 80 new members each year for significant research accomplishments.

Barton F. Haynes, MD, Frederic M. Hanes Professor of Medicine and director of the Duke Human Vaccine Institute, was elected to the American Academy of Arts and Sciences in April. Fellows are selected through a highly competitive process that recognizes individuals who have made preeminent contributions to their disciplines and to society at large.

Samuel Katz, MD, Wilburt Cornell Davison Professor and chairman emeritus of pediatrics, has been awarded the 2007 Pollin Prize.

The prize, which honors one person annually for contributions to pediatric research and to recognize outstanding achievement in biomedical and public health research that improves child health, is the largest international award of its kind monetarily.

Katz was selected for his role in the development of the measles vaccine and for his work to eradicate the disease in resource-poor nations. Katz receives $100,000, along with an additional $100,000 to award as a fellowship stipend to a young investigator working in a related area. Katz has selected **Michael Anthony Moody, MD**, of Duke's Division of Pediatric Infectious Diseases.

Judith Kramer, MD, an associate professor of medicine and member of the Duke Clinical Research Institute, has recently been invited to serve as a member on the Drug Safety and Risk Management (DSaRM) Advisory Committee of the U.S. Food and Drug Administration (FDA). The appointment runs through May 2010. The DSaRM committee is charged with advising the FDA commissioner on risk management, risk communication, and quantitative evaluation of spontaneous reports of adverse events.

David Millington, PhD, professor of pediatrics in medical genetics, received the 2006 Guthrie Award, which honors an individual for achievement in the field of neonatal screening. In the 1980s, Millington pioneered the use of tandem mass spectrometry to detect specific substances in blood samples, eliminating the need for chromatographic separation and allowing efficient diagnosis of inherited metabolic diseases with very small quantities of blood. "Tandem mass spectrometry revolutionized newborn screening and is now commonplace around the country, and it is wonderful to see David honored for his work in this area," says pediatrics chair Joseph St. Geme III, MD.

Raphael H. Valdivia, PhD, assistant professor of molecular genetics and microbiology, was selected as one of two recipients of the American Society for Microbiology Merck Irving S. Sigal Memorial Award.

The award recognizes excellence in basic research in medical microbiology and infectious disease by a young investigator. Valdivia was honored for his established record of creative and independent research in the area of molecular and cellular microbiology.

Seven Duke Medicine faculty members were awarded Duke University distinguished professorships in April. They are:

- **Ann Marie Pendergast, PhD**, James B. Duke Professor of Pharmacology & Cancer Biology
- **Joseph St. Geme III, MD**, James B. Duke Professor of Pediatrics
- **Harvey Cohen, MD**, Walter Kempner Professor of Medicine
- **Ramon Esclamado, MD**, Richard Hall Chaney, Sr. Professor of Surgery
- **Diane Holditch-Davis, PhD, RN**, Marcus Hobbs Professor of Nursing
- **Danny Jacobs, MD**, David C. Sabiston, Jr. Professor of Surgery
- **Salvatore Pizzo, MD, PhD**, Distinguished Professor of Pathology

DUKE UNIVERSITY AFFILIATED PHYSICIANS

Richard J. Schneider, MD
Particular Clinical Interests and Skills: General adult medicine, integrative medicine
Faculty Rank: Consulting Associate
Division: Harps Mill Internal Medicine
MD Degree: Wayne State University School of Medicine, Michigan
Residency: Internal Medicine, Providence Hospital, Michigan, 1976-1979

Ananya B. Sen, MD
Particular Clinical Interests and Skills: Women's health, pediatrics, preventive medicine from newborn to adolescents to geriatrics
Faculty Rank: Consulting Associate
Division: Butner-Creedmoor Family Medicine
MD Degree: Calcutta National Medical College, India, 1988
Residency: Pediatrics, Vivekananda Institute of Medical Sciences
Internal Medicine/ Pediatrics, MetroHealth Medical Center, Cleveland, Ohio, 1998-1999
Family Practice, 2001

MEDICINE

Deverick J. Anderson, MD
Particular Clinical Interests and Skills: Multi-drug-resistant organisms, hospital epidemiology, infection control, hospital-acquired infections including catheter-related bloodstream infections and surgical site infections
Faculty Rank: Clinical Associate
Division: Infectious Diseases and International Health
MD Degree: Duke University School of Medicine, 2001
Residency: Internal Medicine, Duke University Medical Center, 2001-2004
Fellowship: Infectious Diseases, Duke University Medical Center, 2004-2006
Other: MPH, Epidemiology, University of North Carolina at Chapel Hill, 2007

Laurie D. Snyder, MD
Particular Clinical Interests and Skills: Lung transplant, immune mechanisms of transplant rejection, general pulmonary medicine
Faculty Rank: Associate
Division: Pulmonary, Allergy, and Critical Care
MD Degree: Duke University School of Medicine, 2000
Residency: Internal Medicine, University of California, San Francisco, 2000-2003
Fellowship: Pulmonary and Critical Care Medicine, Lung Transplant, Duke University Medical Center, 2003-2006

OB/GYN

Anthony G. Visco, MD
Particular Clinical Interests and Skills: Robotic sacrocolpopexy, robotic hysterectomy, slings and other minimally invasive surgeries for the surgical treatment of pelvic organ prolapse and urinary incontinence, vesicovaginal fistula, urodynamics
Division: Urogynecology
MD Degree: State University of New York in Syracuse, 1993
Residency: University of Rochester, New York, 1997
Fellowship: Urogynecology and Reconstructive Pelvic Surgery, Duke University Medical Center, 2000

OPHTHALMOLOGY

M. Tariq Bhatti, MD
Particular Clinical Interests and Skills: Clinically oriented research interests in optic neuritis and multiple sclerosis, giant cell arteritis, the ophthalmic complications of endoscopic sinus surgery and orbital syndromes
Faculty Rank: Associate Professor
Division: Neuro-ophthalmology Services
MD Degree: New York Medical College, 1993
Residency: Ophthalmology, University of Florida, 1994-1997
Fellowship: Neuro-ophthalmology, Emory University, Georgia, 1997-1998
Orbital Disease and Surgery, Allegheny General Hospital, Pennsylvania, 2004-2005

Dana M. Blumberg, MD
Particular Clinical Interests and Skills: Diagnosis and treatment of glaucoma, medical and surgical glaucoma management
Faculty Rank: Assistant Professor
Division: Glaucoma Service
MD Degree: St. Louis University School of Medicine, Missouri, 2000
Residency: Ophthalmology, Case Western Reserve, Ohio, 2001-2004
Fellowship: Glaucoma, Wilmer Eye Institute, Maryland, 2004-2005

PEDIATRICS

Kathleen A. McGann, MD
Particular Clinical Interests and Skills: Pediatric infectious diseases, human immunodeficiency virus (HIV) infection, pediatric education, general pediatrics
Faculty Rank: Professor
Division: Infectious Diseases
MD Degree: University of Pennsylvania School of Medicine, 1985
Residency: Pediatrics, Children's Memorial Hospital, Northwestern University, Illinois, 1985-1889
Fellowship: Pediatric Infectious Diseases, Children's Hospital of Philadelphia, Pennsylvania, 1989-1992

Peter H. Michelson, MD
Particular Clinical Interests and Skills: All pediatric lung diseases, cystic fibrosis, asthma, obesity, exercise, and airway anomalies
Faculty Rank: Assistant Professor
Division: Pulmonary Medicine
MD Degree: Jefferson Medical College, Pennsylvania, 1983
Residency: St. Christopher's Hospital for Children, Pennsylvania, 1986
Fellowship: UNC Hospitals, Pediatric Pulmonology, 1995
Other: MS, Clinical Research, University of Pittsburgh, 2007

Vandana Nayal, MD
Particular Clinical Interests and Skills: High risk neonates, neurodevelopmental follow-up, neuroprotection, neonatal resuscitation
Faculty Rank: Clinical Associate
Division: Neonatal-Perinatal Medicine
MD Degree: MBBS, Chengalpattu Medical College, India, 1989
DCH, Government Medical College, Nagpur, India, 1993
Residency: Pediatrics, New York Methodist Hospital, 2000-2003
Fellowship: Neonatal-Perinatal Medicine, Oregon Health and Sciences University, 2003-2006

Daniel S. Wechsler, MD, PhD
Chief, Division of Pediatric Hematology-Oncology
Particular Clinical Interests and Skills: Pediatric leukemia and lymphoma, neuroblastoma, histiocytosis
Faculty Rank: Associate Professor
Division: Hematology-Oncology
MD Degree: MDCM, McGill University, Montreal, 1987
Residency: Pediatrics, Johns Hopkins Hospital, Maryland, 1987-1990
Fellowship: Pediatric Hematology-Oncology, Johns Hopkins Hospital, Maryland, 1990-1994
Other: PhD, Physiology, McGill University, Montreal, 1987

Stephanie B. Wechsler, MD
Particular Clinical Interests and Skills: Congenital heart disease occurring as part of genetic syndromes, as well as other cardiovascular diseases with a genetic cause including cardiomyopathies and connective tissue diseases such as Marfan syndrome
Faculty Rank: Associate Clinical Professor
Division: Cardiology
MD Degree: University of Texas Medical School, 1987
Residency: Pediatrics, Johns Hopkins Hospital, Maryland, 1990
Fellowship: Pediatric Cardiology, Children's Hospital, Massachusetts, 1994
Medical Genetics, University of Michigan, 2003

Found in translation: A chat with Robert Califf, MD, director of the new Duke Translational Medicine Institute

LAST FALL, THE NATIONAL INSTITUTES OF HEALTH (NIH) granted Duke $52.7 million over five years to establish the Duke Translational Medicine Institute (DTMI). One of 12 such institutions nationwide, the DTMI is charged with moving scientific discoveries into practical applications that improve human health. On the surface, that sounds like something Duke and other research universities have always done. But Robert Califf, MD, believes the DTMI will spur the often-sluggish process into warp speed.

Califf

Why do we need these new translational medicine institutes?

U.S. taxpayers are paying almost $30 billion a year into the NIH, but our health is no better than that of people in many other countries. For example, Durham County's residents don't live as long and have higher rates of infant mortality, stroke, and heart failure than people in Cuba.

That's due in part to two big blocks in the translational medicine process. The first is our inefficiency in turning a laboratory discovery into a testable technology—a new drug, diagnostic device, or behavioral intervention. The second block comes in deploying a proven technology so that it actually improves people's health. Right now the average time from clinical trials that prove something is effective to fully deploying it is between 10 and 25 years.

We know that discovery science happens best with a genius in the lab pursuing ideas generated through personal curiosity about how nature works. But translating that discovery into something useful is a whole different endeavor. To do that, you need an organized approach to moving from discovery to technology to clinical tests to deployment. That's where DTMI comes in.

And how will this affect the health of our patients—say, those here in Durham?

We have made a bold statement: that we are going to work with the community of Durham to improve the health status of our county. The big bet we are making is that if we work together with the residents of Durham County—not telling them what to do, but through participatory research—we can improve the health of people who live here.

One of our ideas is to offer personal electronic health records to everyone in Durham County, whether they are in the Duke system or not. Then we can see trends and target the best treatments for individuals and neighborhoods at the most reasonable costs. We believe, for example, that within five years, we could see noticeable improvements in health—reducing infant mortality, preventing diabetes complications, lowering stroke rates. But we need to work with the community to determine how best to do this.

This institute is a huge effort. What do you see as the greatest challenge about it?

The challenge is to successfully create a more centralized, project-oriented structure for applied science in the academic world. We often talk about "transactional cost"—the measure of energy it takes to get something done. If, in adding this new layer of effort and administration, we raise the transactional cost, we have failed. If we lower it, we will succeed.

We have a great model of how to do this in the Duke Clinical Research Institute, which is recognized as the best academic clinical research center in the nation and will be a key part of the DTMI. We took decentralized clinical trials and found ways to lower the transactional cost and increase collaboration so that we could improve health. So we know it can be done, and it can make a difference to the health of our community, our nation, and the world.

For more information, visit dtmi.duke.edu.

CONTINUING MEDICAL EDUCATION AT DUKE
For more information on the courses listed below, please contact the Duke Office of Continuing Medical Education at 919-401-1200 or visit cme.mc.duke.edu.

DUKE CME CALENDAR

ON SITE

COURSE	DATE	LOCATION	CREDIT	REGISTRATION
ANESTHESIOLOGY				
2nd Annual Chronic Pain Management Fall Symposium for Primary Care	September 29, 2007	Searle Center Durham, NC	4.5 credits	919-668-2386
Anesthesia Camp IV Laguna Beach	October 3-6, 2007	Montage Resort & Spa Laguna Beach, CA	18 credits	1-888-286-5815
4th Annual Ultrasound Symposium: Ultrasound for Every Anesthesiologist	October 12, 2007	The W Hotel San Francisco, CA	7 credits	siler006@mc.duke.edu
Anesthesia Camp Costa Rica	October 24-27, 2007	Four Seasons Resort Guanacaste, Costa Rica	15.5 credits	1-888-286-5815
INTERNAL MEDICINE				
23rd Annual Internal Medicine Symposium	July 30-August 3, 2007	Hilton Head Island, SC	25 credits	919-668-5947
ONCOLOGY				
Oncology Highlights 2007: Updates from ASCO	July 13, 2007	Durham, NC	6 credits	919-419-5506
8th Annual Hampton Roads Oncology Educational Conference	October 20, 2007	Virginia Beach, VA	6.5 credits	919-419-5506
OPHTHALMOLOGY				
Duke Dinner Series	September 17, 2007	Durham, NC	2 credits	919-684-6593
RADIOLOGY				
MRI at the Workstation	August 11-12, 2007	Ritz Carlton Washington, D.C.	11.25 credits	919-684-7228
MRI at the Workstation	October 6-7, 2007	Ritz Carlton Chicago, IL	11.25 credits	919-684-7228
A Practical Approach to Musculoskeletal MRI	October 13-16, 2007	Las Vegas, NV	20 credits	919-684-7228
Musculoskeletal MRI & Neuroimaging	October 20-23, 2007	The Grove Park Inn Resort & Spa, Asheville, NC	20 credits	919-684-7228
UROLOGY				
Duke Tuesday in Urology	July 17, 2007	Durham, NC	5 credits	919-684-2033

ONLINE

COURSE	DATE	CREDIT	REGISTRATION
RESEARCH ETHICS Social Sciences Research in Medical Settings Protecting the Confidentiality and Privacy of Patients Protecting Research Subjects What Counts as Research with Human Subjects Children Involved as Subjects in Research Ethical and Regulatory Considerations When Bringing a Medication to Market Informed Consent for Research Research in Emergency Settings Using Databases in Research Adolescent Participation in Research Prisoners Involved as Participants	All Research Ethics courses are available through December 31, 2008	Up to 1 credit	For more information or to register, visit: researchethics.duhs.duke.edu
Insertion of Central Venous Catheters	Through December 13, 2007	2.25 credits	cvctraining.medicine.duke.edu
Web Archive: 12th Annual Duke ACS Symposium	Through February 27, 2008	2.25 credits	thrombosisclinic.com/en/11/39/6688/

CD-ROM

COURSE	DATE	CREDIT	REGISTRATION
The LIFE Curriculum: Learning to Address Impairment and Fatigue to Enhance Patient Safety	Through August 31, 2007	1 credit	lifecurriculum.info
Improving the Recognition of Wearing-Off in Parkinson Disease	Through September 14, 2007	1.5 credits	medicus.international@medicusgroup.com
Defining Foundation Antithrombin Therapy	Through September 14, 2007	1 credit	212-866-3122

These activities have been approved for AMA PRA credit.

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When gain means pain.

Nearly three times as many American youth are overweight today as just a generation ago. And along with excess weight, they're piling on health problems—like type 2 diabetes, joint pain, and hypertension. "These are not traditional childhood illnesses, and frankly most pediatricians aren't trained to treat them," says Sarah Armstrong, MD (right). "If you've got to talk to your patient about asthma and that he's failing math and that he's overweight and that his cholesterol is getting too high, all in a brief office visit—at some point something's going to have to give." As director of Duke Children's new Healthy Lifestyles Program, Armstrong is working to support fellow pediatricians—and save the health of a generation.

Read more on page 24.

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