VOLUME 6
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DukeMed MAGAZINE

Scientific solutions

Bringing patients the benefits of biomedical research

Serious about science

This September, Duke Medicine hosted a landmark event: our 75th Anniversary Science Symposium. The symposium brought together a brilliant group of scientists, both accomplished and aspiring, who came from Duke and around the nation to attend. Any time we have so many gathered in one place to celebrate and discuss science it is invigorating, and the theme for this occasion was particularly inspiring: "Science's Next Great Idea."

Pursuing great ideas is what Duke investigators do every day. In this issue of *DukeMed Magazine*, you can read about some of our physicians and scientists who are translating their research discoveries into new treatments for illnesses across the spectrum of human health—from exploring innovative heat-based therapies for cancer, to leading efforts to develop an HIV/AIDS vaccine and improve medical care for current sufferers at home and abroad to developing a lifesaving treatment for the genetic disorder Pompe disease. These stories are just a sampling of how Duke's investigator-driven research can lead to scientific advances that bring healing and hope to the sick and improve health around the world.

Duke's science, both curiosity-driven and disease-based, encourages us to be inquisitive, to challenge paradigms, and to solve fundamental scientific mysteries. But achieving success also takes the dedication of time and resources at personal, professional, and institutional levels.

I believe that Duke Medicine has both the potential and the duty to set the pace for creating, sharing, and using new knowledge and new discoveries. By doing so, we will make a difference in our community and around the world.

For this reason, we announced at the Science Symposium a number of initiatives designed to strengthen science at Duke. They include the creation of a Science Advisory Council composed of Duke researchers, and a Scientific Advisory Board of leading researchers from outside our institution. In the coming months, these groups will generate ideas and provide guidance as we move Duke science forward.

I believe that Duke Medicine has both the potential and the duty to set the pace for creating, sharing, and using new knowledge and new discoveries. By doing so, we will make a difference in our community and around the world.

We also announced a transfer of $280 million from our health system reserves to support research and education. This historic transfer offers our academic efforts unparalleled financial stability in a time of shifting government budgets and unpredictable markets. It enables us to move forward with the strategic plans of the Schools of Medicine and Nursing. It also gives us much-needed support for investigator-directed basic discovery and clinical research activities, which are vital for advancing knowledge, education, and training.

Our plans are ambitious, and while good investment growth over the past few years has enabled this one-time transfer to support academics at Duke, achieving our ambitions will continue to require funding from government, industry, and other organizations, as well as the generous philanthropic support of our friends and donors. Yet by establishing this fund we are saying, in a very concrete way, that we are serious about our commitment to science.

Wilburt C. Davison, MD, the first dean of the Duke University School of Medicine, came to Durham to build an institution that would use science to advance medicine. The people he hired shared his passion, and over the last 75 years researchers at Duke have significantly advanced medicine through basic discovery, public health policy, and everything in between.

We hope that Duke Medicine's public commitment to science will encourage and inspire donors to join with us as we seek to transform medicine. By working together, we can ensure that our next 75 years will be even more productive and exciting, and that Duke Medicine will continue to be recognized as an institution where science provides a strong foundation for the study, practice, and advancement of medicine.

VICTOR J. DZAU, MD
PROFESSOR OF MEDICINE
CHANCELLOR FOR HEALTH AFFAIRS,
DUKE UNIVERSITY
PRESIDENT AND CEO,
DUKE UNIVERSITY HEALTH SYSTEM

DukeMed MAGAZINE
VOLUME 6, ISSUE 2, FALL/WINTER 2006

The long hunt

Twenty-five years after the first AIDS diagnosis, scientists are taking research in new directions—with the goal of closing in on a vaccine at last.

The making of a miracle

How a Duke scientist's passion translated into a lifesaving treatment for Pompe disease—a genetic disorder that once killed every baby it touched.

Hot stuff

An ancient approach to tumor treatment is making waves in 21st-century cancer care.

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A fresh face

NOTICE ANYTHING NEW ABOUT *DUKEMED MAGAZINE*?

With this issue, we've made some design changes to reflect the launch of a new Duke Medicine brand. An overarching name that represents the total scope of Duke's health-related entities and endeavors, "Duke Medicine" will be appearing everywhere from building signage and business cards to publications and print ads to a new series of television spots beginning in January 2007.

As part of the campaign, we're introducing a signature look for Duke Medicine. It features a streamlined typeface, contemporary color palette, and modern design elements, including gradient color bars intended to symbolize the synergistic relationship among Duke's research, education, and clinical care missions and to convey a sense of progress. (See what you can learn from chatting with graphic designers?)

DukeMed Magazine already sported a modern design, in keeping with our purpose of communicating current events and advances at Duke Medicine. Accordingly, the changes to this magazine are fairly subtle—Botox versus a full facelift. But we think the refreshment is, well, refreshing…and a good reflection of this forward-facing, ever-evolving institution.

Before

After

Let us know how you like the new look—and the rest of the magazine—by filling out the reply card inserted into this issue. You can also write to us at DukeMed Magazine, Duke Medicine Office of Creative Services, DUMC 3687, Durham NC 27710, or send an e-mail to dukemedmag@mc.duke.edu. We look forward to hearing from you.

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WILL MCINTYRE

from the dean

Nourishing research in lean times

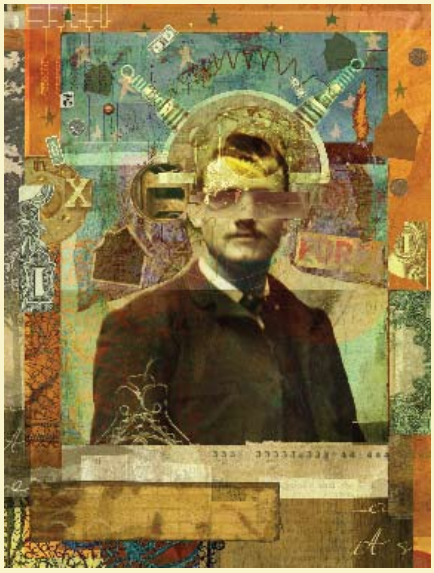
by R. Sanders Williams, MD
Dean, Duke University School of Medicine
Founding Dean, Duke-NUS Graduate Medical School Singapore
Vice Chancellor for Academic Affairs

In recent years the growth of federal support for biomedical research overall has come to a virtual standstill. Yet support for Duke medical research has increased significantly—over the past five years, Duke has risen from 11th to fifth among all medical schools in the rankings of NIH funding.

DURING MY YEARS as a practicing cardiologist, I often stood at the bedside of a critically ill patient with nothing left to offer except reassurance to the family that every known therapeutic measure had been employed. At such times I yearned for more knowledge and better technology that might have rescued my patient or, better still, prevented their progression to the end stage. Most physicians have had similar experiences, and they often make a lasting impact. For me, and for many of us here at Duke Medicine, the emotions generated by such encounters joined with an innate curiosity about the workings of the molecules and cells of the human body to direct our career paths towards research.

The faculty, staff, and students of Duke Medicine do a great deal of research, and they do it very well indeed. At least 500 of our faculty serve as principal investigators on research grants, with hundreds more graduate students, post-doctoral fellows, and medical students engaged in such studies as well. Collectively, we spend over $450 million annually to conduct research. While endowment, philanthropic gifts, and investments from our clinical enterprise provide important support for these efforts, more than 85 percent of the funding comes from industry or U.S. government sponsors, primarily the National Institutes of Health.

Securing NIH funding is not easy. Our grant proposals are judged by peer reviewers in an open and fierce competition with investigators from other schools. Moreover, in the past two years, the growth of federal support for biomedical research has come to a virtual standstill. In the most recent NIH fiscal year, its budget grew by only 2 percent—an actual decline in purchasing power. Yet, remarkably, support to Duke medical faculty grew by about 14 percent, to some $350 million. Since 2001, Duke has risen from 11th to fifth among all medical schools in the rankings of NIH support. Over the same period our School of Nursing has moved from 44th to 19th.



How have we done so well during these relatively lean times? Personally, I believe it has been by remaining true to a few basic principles that put us in a strong position to advance our research mission. First is the belief that excellence in research is a defining element of Duke Medicine, one worthy of sacrifice to achieve. This belief permeates our institution, and is championed even by those who have little direct involvement in research activities—as evidenced by the recent transfer of $280 million from our health system to support research and education.

Second, Duke has a superior environment for building research teams. When I began my research career in the 1970s, biomedical research was considered a solitary art, but today the most important findings often come from teams of investigators. At Duke, such signature programs as our Global Health Institute and Translational Medicine Institute both illustrate our dexterity for teamwork and lay the groundwork for our continuing leadership in this arena. [Read more on pages 4 and 64.]

Finally, our success rests on gifted faculty members who choose to do their work here— both because of the rich intellectual climate, and because Duke strives to provide an environment in which success is limited only by one's own energy and talent, and not by internal constraints.

Of course we must constantly reaffirm these ideals in order to realize them. Our Strategic Plan (online at dukehealth.org/vision) calls for a number of new measures to help us continue to place a priority on research, strengthen research teams, and support individual innovation. With our commitment secured, I have no doubt we will be able to continue to excel in research, and to offer new hope to the patients we will stand before in the future.

A new era of discovery

DUKE MEDICINE will supercharge its bench-to-bedside strengths by establishing the Duke Translational Medicine Institute, backed by a $52.7-million grant from the National Institutes of Health. The five-year grant is one of 12 such grants totalling $699.5 million to educational institutions nationwide. The NIH, in its first systematic change of approach to clinical research in the last 50 years, is developing a consortium of "discovery engines that will improve medical care by applying new scientific advances to real-world practice," says NIH director Elias Zerhouni, MD.

"As a result of this NIH program, Duke investigators and physicians will have the support to bring innovative therapies to our patients in a timely and efficient way, in the same manner as our researchers are making basic science discoveries in the laboratory," says Victor J. Dzau, MD, chancellor for health affairs of Duke University and president and CEO of the Duke University Health System.

The NIH plans to award additional grants through its Clinical and Translational Science Award program to widen the consortium to 60 institutions by 2012. Duke's programs are headed by Robert Califf, MD, vice chancellor for clinical research and former director of the Duke Clinical Research Institute. "This grant will foster speedier delivery of new treatments and health care practices to the community," Califf says. "We hope to involve the individual person and families in preventing illness and coping with existing illness in a way that has been only a dream in the past."

The Duke Translational Medicine Institute will be the administrative umbrella for a diverse group of new and existing Duke entities:

- The **Duke Clinical Research Institute**, established in 1969, which organizes and manages large-scale international clinical trials, disease registries, and health outcome studies
- The new **Duke Clinical Research Unit**, which will combine the current General Clinical Research Center, a federally funded inpatient unit specializing in novel clinical research, with a new facility to treat patients enrolled in first-time trials of new drugs, devices, and vaccines
- The Duke **Translational Research Institute**, to be developed with the new NIH grant, to streamline the process of guiding new scientific discoveries through the early phases of development into technologies that can be applied to human health
- The new **Duke Community Clinical Research** unit, which will combine current efforts with new initiatives to create a model system to improve overall health status in Durham County while developing collaborations locally and internationally to discover the best models of preventing and treating illness on a community-wide basis.

> "[The new $52.7-million NIH grant] will foster speedier delivery of new treatments and health care practices to the community. We hope to involve the individual person and families in preventing illness and coping with existing illness in a way that has been only a dream in the past."
>
> —Robert Califf, MD, director of the new Duke Translational Medicine Institute

The new institute also will coordinate efforts in translational medicine at the North Carolina Research Campus, being developed in Kannapolis, North Carolina, and the recently established Duke-National University of Singapore Graduate Medical School, located in Singapore. In addition, it will provide comprehensive education and training for students and health-care professionals in the complexities of translational and clinical research. "We will build on the principle that a rich clinical and translational research environment provides trainees with models and opportunities for success," Califf says. "We envision training the next generation of leaders in translational medicine."

Making a big bang in science

THE 75TH ANNIVERSARY SCIENCE SYMPOSIUM brought top researchers to the Duke campus to inspire students and faculty and to recognize the contribution of science to the medical center's success. The September event was a Big Bang: two days in which 13 notable scientists, including three Nobel laureates, spoke to the theme of "Science's Next Great Idea," sharing wisdom, ideas, and experimental results.

"Biologists love details, but they can lose the bigger picture because of this."

—Nobel Laureate Paul Nurse, PhD, encouraging attendees of Duke's 75th Anniversary Science Symposium to think of biology in terms of networks, not just straight-line pathways. Nurse, who is president of the Rockefeller University in New York City, gave the keynote address for the symposium.

Among the speakers were Yale's Richard Lifton, MD, PhD, who studies genetic mutations associated with hypertension; Helen Hobbs, MD, of the University of Texas Southwestern, who studies the genetics behind cholesterol levels; and Carol Greider, PhD, of Johns Hopkins, who discovered and has since spent more than 20 years characterizing an enzyme that maintains the ends of chromosomes. Greider was recently awarded the Lasker Prize for Basic Medical Research, considered by many to be the "American Nobel."

Bruce Stillman, PhD, president and CEO of the Cold Spring Harbor Laboratory, emphasized the need for a balance of basic research and applied research. Bruce Alberts, PhD, former president of the National Academy of Sciences, shared his belief that it is critically important that scientifically trained people be in all professions, so that science can achieve a much higher degree of influence both within nations and around the world.

Many of the speakers, including Joseph Goldstein, MD, whose plenary lecture closed the symposium, highlighted the importance of mentors. Goldstein, the chair of molecular genetics at the University of Texas Southwestern Medical Center in Dallas, also advised young scientists that, to develop science's next great idea, it would be essential to take chances, by letting go of assumptions, ignoring conventional wisdom, and being willing to speculate. "The symposium created a buzz of excitement," says medical school dean R. Sanders Williams, MD. "Now we need to run with it."

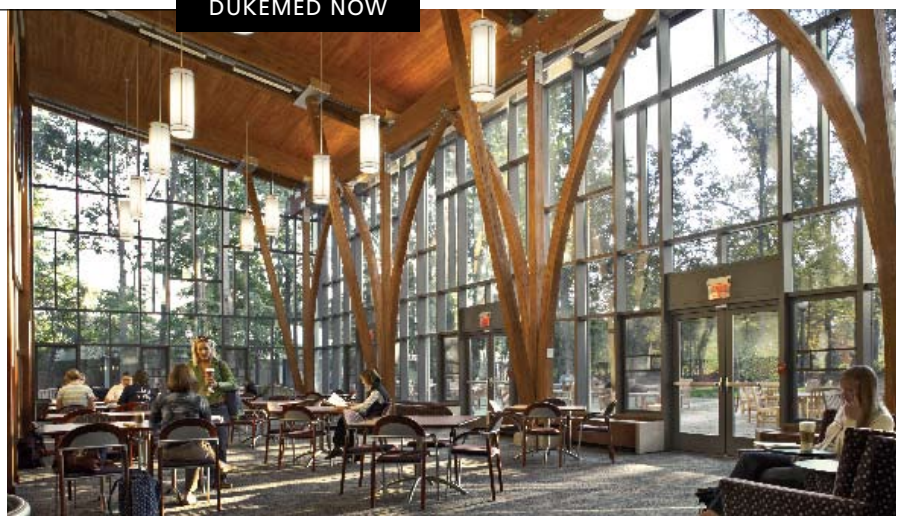
Investing in academics

THE 75TH ANNIVERSARY Science Symposium was a fitting occasion at which to announce a new and profound boon for Duke Medicine researchers and students. Victor J. Dzau, MD, chancellor for health affairs of Duke University and president and CEO of the Duke University Health System (DUHS), announced at the September symposium the establishment of a $280-million academic fund to support research and education programs at Duke's schools of medicine and nursing. The fund has been provided in the form of a one-time transfer from the health system's reserves, which have grown substantially in recent years due to strong investment performance.

Since its creation in 1998, DUHS has transferred $20 to $30 million annually to the academic program. This transfer represents a 10-year pre-payment that will facilitate long-term planning and provide investment income. Dzau told the audience that the $280 million, and the interest it earns, will be drawn from over the next decade to fund research and education programs at Duke University Medical Center, including new discovery science, translational science, and health disparities research initiatives.

"We're making this investment in research and teaching so that patients at Duke will continue to have access to the most advanced care that medicine has to offer," says William J. Fulkerson, MD, CEO of Duke University Hospital and DUHS vice president for acute care services. "The strength of our clinical programs will always be tied to the commitment that we are willing to make to our complementary missions of teaching and research."

Read more on the inside front cover.



New faces, new spaces: Duke's first nursing PhD students began their studies in the brand-new School of Nursing building, a stunning 56,000-square-foot facility opened this summer on Trent Drive.

Duke School of Nursing launches PhD program

AS SCHOOLS OF NURSING around the country struggle to find qualified faculty and providers seek better ways to meet the complex needs of the chronically ill, doctorally prepared nurses are in increasing demand. With the start of the academic year, Duke welcomed a group of students who will soon be able to help meet those needs—its first class of nursing PhD candidates.

More than 32,000 qualified baccalaureate-level applicants were turned away from nursing schools in 2004 because of a lack of faculty to teach them.

"More than 90 million Americans currently live with chronic illness, and they account for more than 75 percent of our nation's $1.4 trillion in medical care costs," says Duke Chancellor for Health Affairs Victor J. Dzau, MD. "High-quality nursing science is needed to improve health outcomes for these individuals and their families."

The new PhD program at Duke is a tremendous investment, but one that is vital to continue the steep rate of research growth targeted by Catherine L. Gilliss, DNSc, RN, FAAN, dean of the School of Nursing and vice chancellor for nursing affairs. The school will cover full tuition for each student, plus a stipend, for a total cost of $50,000 each.

"This program addresses both the need for evidence-based models of care and the shortage of doctorally prepared nurse educators," says Gilliss. "It is an investment in our school and the community we serve."

The PhD program will prepare nurse scientists to conduct research that follows people with chronic illness and their interactions with care systems over time. The goal is to design interventions to improve health outcomes and also to prepare nurses for positions in academics.

The shortage of nursing faculty is felt at all levels of nursing education.

More than 32,000 qualified baccalaureate-level applicants were turned away from nursing schools in 2004 because of a lack of faculty to teach them. At the master's level, the shortage of community college faculty prevents rural nurses from advancing their education to increase the level of community-based care they can provide.

"People choose the field of nursing because of nursing practice," says Ruth Anderson, PhD, RN, FAAN, director of the new PhD program. "Many people aren't aware of the opportunities in nursing science, but it is increasingly needed and valued to improve health care."

The Duke program is small and individualized with an emphasis on faculty mentoring. Anderson was encouraged by the many strong applications she received from potential students. The interests of those selected vary from chronic illness-related health care delivery systems to patient safety. Plans call for a second cohort of four students in 2007-08 and six in 2008-09.

Prior to establishing the program, Duke was the highest-ranked nursing school in the country without a PhD program. It joins 88 other nursing PhD programs nationwide.

Excerpted from the Spring/Summer 2006 inaugural issue of the DukeNursing Magazine. *To download the complete magazine, visit development.mc.duke.edu/nursing/nurseAlum/index.htm.*

Duke nurses: Simply magnetic

DUKE UNIVERSITY Hospital can add magnetic appeal to its national stature. This September, the American Nurses Credentialing Center (ANCC) officially named Duke a Magnet Hospital, a designation only 3.7 percent of the nation's hospitals have earned.

The ANCC, the credentialing arm of the American Nurses Association, lists four objectives for the Magnet Recognition Program:

- Recognizing hospitals that deliver excellent nursing care to patients,
- Promoting quality in an environment that supports professional nursing practice,
- Disseminating successful nursing practices among health care organizations, and
- Promoting positive patient outcomes.

The award culminates a three-year application and evaluation process, says Mary Ann Fuchs, MSN, RN, chief nursing and patient care services officer for Duke University Hospital and Health System. The assessment included interviews with more than 500 nurses, physicians, and staff, as well as examination of nearly 3,000 pages of documentation. Magnet designation lasts four years, and helps the hospital attract and retain the best-trained nurses. Nurses who work in these institutions are also allowed to spend more individual time with patients—factors that can lead to shorter hospital stays, according to ANCC.

"This is the highest honor a U.S. hospital can receive for its nursing program, and it recognizes the innovative, first-rate care patients receive at Duke," says Chancellor for Health Affairs Victor J. Dzau, MD. "Achieving magnet status is a testament to the knowledge and dedication Duke nurses bring to their profession."

TED BYRNES

3,000 PAGES documenting its excellence in nursing helped Duke University Hospital earn Magnet status—something fewer than 4 in 100 American hospitals have achieved.

Nurses across Duke Medicine have made the grade this year: In addition to Duke University Hospital's new Magnet status, both the Davis Ambulatory Surgery Center at Durham Regional Hospital and Duke Raleigh Hospital earned Healthy Workplace recognition this fall. Duke Raleigh is the first hospital in the state to earn the Hallmarks of Healthy Workplace designation by the North Carolina Nurses Association Professional Practice Advocacy Coalition (NCNA). The recognition goes to facilities that have developed healthy workplaces for nursing staff and advocate nursing involvement in all facets of the organization.

A pearl of a hospital—especially this year

OCTOBER 3, 2006 marked Durham Regional Hospital's "pearl" anniversary. The hospital, originally Durham County General Hospital, was created 30 years ago through a merging of two local hospitals, Lincoln and Watts. In 1990, as the once-small Durham community exploded into a sprawling region, the hospital expanded its service area and was rechristened Durham Regional Hospital (DRH). In 1998, DRH became part of the Duke University Health System (DUHS) through a 20-year lease agreement between DUHS and the Durham County Hospital Corporation.

Read more about the anniversary celebration at durhamregional.org.

That's LIFE: Improving patient care through physician wellness

MEDICAL STUDENTS WORK hard for four years, making social, familial, and physical sacrifices not often called for in other professional training programs. They tax their intellects and emotions to their limits, doing whatever is necessary to master their coursework and retain the oceans of information flooding their minds.

And then comes residency.

Stress and fatigue cannot be avoided during the rigorous training of young doctors. "Physicians experience stressors that put them at risk for fatigue, impairment, and burnout in ways that other professionals are not," says Kathryn Andolsek, MD, MPH, associate director of graduate medical education at Duke. "Evidence shows that serious problems with impairment start early in medical training." Andolsek, an emphatic advocate of the relationship between patient outcomes and the well-being of health-care providers, says that residency directors must make sure these new generations of physicians are caring for themselves, so that they are in an appropriate condition to care for their patients.

TO LIFE: In 2002 the ACGME (Accreditation Council for Graduate Medical Education) mandated education for all interns, residents, fellows, and faculty about fatigue and impairment. So Andolsek and the UNC School of Medicine's Robert Cefalo, MD, PhD, recruited a committee of other North Carolina residency program leaders to help design educational content specific to the stresses inherent in physician training. They amassed local and national expertise—from senior professors and practitioners to medical students and residents themselves—to create the LIFE Curriculum. The Josiah Macy Jr. Foundation has granted nearly $1 million over three years for the project.

The curriculum consists of workshops on 12 topics: fatigue, disruptive behavior, stress and depression, substance abuse, burnout, boundary violations, impairment, giving effective feedback, generational issues, recruiting the right applicants, maintaining the appropriate program director role, and legal challenges. Andolsek conducts workshops locally and at national and international conferences. There also is a comprehensive Web site and a free CD-ROM set that contains all the workshop material: trigger vignettes, in which an impairment scenario is enacted with two different courses of action; transcripts of these scenarios to allow role-playing; educational content on each topic; and a teaching guide to allow programs to create their own workshops close to home.

HOT TOPICS: Of all the topics, Andolsek says fatigue and disruptive behavior are the issues that attract the most attention. She also says that she, too, learns a lot from conducting the workshops. "Once I showed the disruptive physician tape [in which a physician berates a nurse, in front of a patient's open exam-room door] to a group of very young doctors in training. The conclusion of that group was that there was nothing wrong with the physician's behavior. It ended up being a very different discussion than I expected.

"In another workshop we discussed the substance-abuse trigger tape, in which a physician asks his colleague for a narcotic prescription. The group couldn't believe that would actually happen. So I asked what they would say if a colleague asked them for a pack of birth control pills or a Z-pack for her bronchitis. Everyone said those things would be fine—but actually it's a violation of North Carolina Medical Board rules for a physician to prescribe outside the formal doctor-patient relationship."

PAYING ATTENTION: The objective of the LIFE Curriculum is to help physicians and residency programs sort through potential issues proactively, so that they know what their policies are, what resources are available,

"Physicians experience stressors that put them at risk for fatigue, impairment, and burnout in ways that other professionals are not," says Duke's Kathryn Andolsek, MD, MPH, who helped create a new curriculum to promote physician wellness.

and what problem areas are helpful to think through before problems arise.

"We can't anticipate everything," says Andolsek. "But in the case of Duke, we have about 900 residents—that's the size of a small town. One could anticipate that the same kinds of things that go on in any other group of 900 people will eventually happen among the residents. Not all on the same year or in the same program, but if you're not finding any residents with these issues in a hospital of that size, then you're probably not looking closely enough."

Physicians can earn CME credit for participating in the LIFE Curriculum workshops or completing the CD-ROM set, which is free and can be ordered online. For more information, visit www.lifecurriculum.info.

Tips to fight fatigue

If a trauma surgeon drank four beers before going into emergency surgery, it's likely that surgery would be her last. Not so if she operates after 24 hours of sleeplessness—even though her brain probably has the functioning capacity of a person who is legally drunk. The 80-hour duty restrictions are designed to avoid having fatigue-impaired physicians treating patients, but anyone who works 80 hours a week will experience some fatigue.

There are strategies that can be employed to minimize the effects of sleepiness and maximize the benefit of the sleep physicians *do* get. In the LIFE Curriculum, sleep expert David Dinges, PhD, of the University of Pennsylvania, offers many suggestions for doctors and others who take overnight call or work night-float shifts:

- **Don't expect to acclimate to night shifts:** Working more nights in a row doesn't help you adjust—it just makes you more tired. Residents should have two 24-hour periods off in a week during which they work a night shift, and they should spend a lot of that time sleeping.
- **Treat caffeine as a drug, not a ritual:** Caffeine is an effective stimulant, but only when you drop your daily Starbucks habit. To benefit from a caffeine boost, ingest caffeinated beverages only when you are working outside your normal sleep schedule—drink it before you feel sleepy.
- **Nap prophylactically:** Taking a nap (15 to 45 minutes) *before* you feel tired can help ward off incapacitating fatigue. Dinges recommends timing naps as closely as you can to normal circadian rhythms: Take an afternoon nap before night-float shifts, and avoid napping between 8 and 10 p.m. if possible. It's also good to try to nap before driving home post-call.
- **Be aware of impairment due to sleep inertia:** That groggy and disoriented feeling that can come with sudden wakening is a neurological condition called sleep inertia. Whenever possible physicians should allow 15 to 30 minutes after waking for their brains and bodies to shake off this compromised mental and physical state. Stand up, turn on the lights, and get moving.

Outpatient pediatrics: Where the revolution begins

THE HEYDAY of manila folders, stuffed fat with reams of paper and shuttled from one doctor's office to another, will soon be a memory at Duke Medicine. Instead, medical records will be just a mouse-click away from physicians and nurses throughout the health system.

The Pickett Road and Southpoint pediatric clinics are the first of Duke Medicine's outpatient clinics to launch the Ambulatory Electronic Medical Record (AEMR) initiative. The initiative is transforming the way medical records are maintained and accessed for thousands of patients across Duke Medicine in an effort to improve patient safety, continuity of care between inpatient and outpatient settings, and patient satisfaction. It also will allow Duke to see trends across large outpatient populations and use that information to improve care on a system-wide basis.

SCRAPPING THE CHICKEN SCRATCH

Struggling to read a handwritten prescription or medical order is frustrating, but it can also be dangerous. Handwritten orders allow for potential mistakes such as transcription errors, transposition, or misreading of drug doses. That's why Duke University Hospital implemented Computerized Physician Order Entry (CPOE) in 2004—and, as of this June, CPOE went live in its first patient care unit at Durham Regional Hospital (DRH), as well. DRH is continuing to roll out CPOE, unit by unit, over two years. Some of the benefits of Computerized Physician Order Entry are:

- **Improved operational efficiency.** CPOE reduces the number of verbal orders given and thus reduces turnaround time for completion of orders and administration of medications.
- **Fewer transcription errors.**
- **Online clinical checking** during the order entry process, which aids in the reduction of medication errors and adverse drug events.

Duke Medicine chose to launch the AEMR in general pediatrics because, until now, that system has been almost totally paper-based. "The first step was to roll out e-prescribing," says Roman Perun, director for the AEMR program. "This system allows us to keep track of all the medicines prescribed to a patient, no matter which clinic they were seen in. This is very important for patient safety."

The e-prescription system also eliminates those scribbled scraps of prescription pad paper tucked into diaper bags and purses. "We enter the prescription into the computer, and it can fax the prescription directly to the pharmacy for the patient," says Vicki Davis, a nurse at Pickett Road. "Patients love it. It is also very convenient for parents who need to get copies of prescriptions for schools or travel. We used to have to physically track down the chart to find the information. Yesterday I had a parent call in for the information and by the time she drove over, we had printed off the prescription."

In addition to e-prescribing, the initial rollout of AEMR has nurses entering vital signs directly into the computer system. So in addition to the bright pictures on the walls and the standard suite of stethoscopes and blood pressure cuffs, each patient room now has a computer hovering out from the wall on a movable arm. "The system talks to the scheduling system, so we can walk into the room, log on, and pull up the patient's name very quickly," says Angela Berry, RN. "We enter the basic reason for the visit, the height and weight, et cetera. One of the benefits is that the computer will now automatically chart a child's growth—we don't have to do those calculations anymore."

For the physicians, having access to electronic records is not a novel experience—many use them when making inpatient rounds. But having a computer in the exam room with a child is. "We were originally concerned about how natural it would be," says Sara Robert, MD. "We usually have a lot of chatter with our patients. We were worried that we wouldn't get that while we were logging on and looking at vital signs and such on the computer. But we are adapting. And the parents and kids think it is wonderful—they wonder why we didn't have computers in the exam rooms before."

Duke Medicine: Now in more neighborhoods

The health needs of North Carolina's ever-swelling population continue to expand, and Duke Medicine keeps growing to fulfill them. Here are some of our most recent additions.

Durham breathes easier

Opened in August, the Asthma, Allergy, and Airway Center in Durham serves all patients with chronic breathing problems. It features laboratories for clinical and basic research, as well as specialized clinical care for adults and children with allergic and airway diseases such as asthma, emphysema, and bronchiectasis. "We're enabling caregivers well-versed in allergic and airway diseases to see patients in a very specialized environment," says director Monica Kraft, MD. "Duke is the first academic medical center in the Carolinas to create a multidisciplinary center to treat these problems."

Duke Asthma, Allergy, and Airway Center • 919-620-7300

Lumberton's hometown heart team

There's an influx of experts to heal the hearts of Lumberton. Duke is now the exclusive provider of heart services at the community's Southeastern Heart Center and two members of Duke's top-ranked heart team have made Lumberton their home address: cardiologist Sydney Short, MD, and cardiothoracic surgeon Terry Lowry, MD, who offers expertise in thoracic as well as heart surgery. "We're making such rapid advances in heart care—it's exciting to be able to bring those benefits to the people we serve," says Short.

Duke Cardiology of Lumberton • Duke Cardiovascular Surgery of Lumberton • 910-671-6619

GI endoscopy at Brier Creek: convenient and less costly, too

The Duke Medicine Gastroenterology Center at Brier Creek makes its home in one of Wake County's hottest new golf-course communities. The center offers general procedures including upper endoscopies and colonoscopies, with a focus towards colorectal cancer screening. "There's a high demand for this type of facility, not only for patient convenience, but also because the copay for these procedures is lower when they're performed in an ambulatory setting," says medical director Stan Branch, MD. The clinic opened this summer next door to a new Duke Medicine family practice.

Duke Medicine at Brier Creek • Gastroenterology services: 919-668-1248 (referring physicians), 919-684-6437 (patients) • Family medicine practice: 919-484-8345

Mental health care in Cary

Residents in Cary have a Duke resource for comprehensive mental health care services. Duke Psychiatry Specialty Clinic in Cary serves adults, adolescents, children, and families, offering psychopharmacologic and behavioral treatment approaches for depression, anxiety disorders, alcoholism and substance abuse, addictive disorders, attention-deficit disorders, schizophrenia, and bipolar disorder. The fee-for-service clinic is located in a private office park and welcomes both self-referrals and physician referrals.

Duke Psychiatry Specialty Clinic in Cary • 919-238-0008

Strong vocals in the City of Medicine

The new Duke Voice Care Center brings together three otolaryngologists, two speech pathologists, and a singing voice specialist to help patients with complex voice, swallowing, and airway disorders. "These problems can have a devastating impact on patients' lives, both professionally and socially," says otolaryngologist Seth Cohen, MD. "Our collaborative approach can return patients to a high level of function." In addition, professional vocalists can learn techniques to preserve and improve their voice quality and projection.

"People often think nothing can be done for voice problems," says center director David Witsell, MD. "It does take an interdisciplinary team to properly treat a disorder, but our patients are often astonished with the results."

Duke Voice Care Center • 919-681-4984

Speed-healing wounds in Wake County

For wounds beyond a Band-Aid solution, patients now have the Wound Healing Center at Duke Raleigh Hospital. The center cares for non-healing wounds, severe infections, diabetic foot ulcers, serious cuts or burns, and snake or spider bites. Specially trained physicians, nurses, and therapists use advanced techniques to diagnose and treat serious and chronic wounds. "This kind of comprehensive, multidisciplinary wound-care service was previously unavailable to patients in Wake County," says medical director D. Scott Covington, MD.

Wound Healing Center at Duke Raleigh Hospital • 919-862-5573

A new Web tool makes it easy for patients to find Duke Medicine locations near them. Check it out at **dukehealth.org/locations**

Construction update

Between April and November 2006, five major construction projects were completed on Duke's medical campus, from a new facility for the School of Nursing to new lab buildings. "It's been a busy year," says Gregory Warwick, Duke Medicine's campus architect. "But we expect more to follow. Our recently completed Campus Framework Plan proposes significant new building over the next decade as we strive to provide our patients and employees with the environment they deserve." In the meantime, here's what's happening now in the construction junction…

THE BIG BOOM

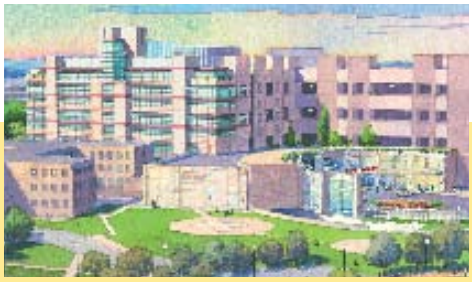
"Mighty Duke" added a curiously long boom to the Duke University Hospital landscape this summer. The super-sized crane—the largest hydraulic crane in North Carolina—was needed to build the new Life Flight helistop on top of the five-story Duke University Hospital ancillary building, part of the ongoing renovation and expansion of the Emergency Department (to be completed in March 2007). Once it is assembled, the crane, operated by Edwards Crane Inc., is 57.9 feet long and 32.1 feet wide, and it weighs 212,000 pounds. The very top of the crane reaches 440 feet skyward—higher than a 20-story building.

LABS GO GREEN

Laboratory buildings are inherent energy hogs, says Gregory Warwick. "Typically the science going on inside doesn't lead to environmentally friendly use of daylight, water, or even air circulation," he says. But Duke and Hillier Architecture of New Jersey have created and opened the Medical Science Research Building II (MSRB II)—a five-story, 160,000-square-foot laboratory facility located on Research Drive—that gives researchers, faculty, and students the high-quality lab spaces they need, while staying in line with Duke's campus-wide green principles.

In fact, by using a wide range of sustainable systems and materials—from the position of the building on site to the use of a heat-recovery wheel, which reduces the amount of energy needed to heat and cool the building—MSRB II will use 26 percent less energy than a similar lab building. That's enough to power 70 average-sized homes for a year, and it will save Duke more than $150,000 annually.

Reprinted from *Sustainability@Duke*



GREEN-LIGHTED AND GOING

The State of North Carolina recently approved approximately $70.6 million for a Duke University Hospital construction and renovation plan that began June 26 and will proceed in three distinct phases:

1. Constructing an eight-story hospital addition and upgrading power and cooling systems
2. Outfitting vacated office space to be new quarters for pre-op holding and the Post-Anesthesia Care Unit (PACU); creating a large, new family waiting room
3. Renovating and modernizing 11 operating rooms.

The plan will increase the number of recovery bays to 70, increase the number of operating rooms to 35, and create more space to accommodate patients and families. The project is directed by Duke Medicine's campus architect's office; Perkins Eastman is the project architect.

STAKING A CLAIM IN A SCIENCE SUPERNATION

The Singapore government drew the rapt attention of the science world when it launched its $4.4-billion commitment to accelerating development in the biomedical sciences. Part of that commitment is Biopolis, a $300-million city-within-a-city that will house academic research institutes, life-science companies, and pharmaceutical research labs.

Now Duke has some acreage nearby, as it broke ground this fall for the construction of the Duke-National University of Singapore Graduate Medical School (GMS). The Singapore government is providing $310 million over seven years to establish the new school, a collaboration between the two institutions aimed at educating future physicians and promoting biomedical research. The school's curriculum is patterned after that of the Duke University School of Medicine, and R. Sanders Williams, MD, dean of Duke's medical school, is serving as founding dean of the new institution. Students are now being recruited for the first class, which matriculates in fall 2007.

Tony Chew, chairman of the GMS governing board, says the school's permanent facility is expected to be completed in summer 2009 and will include 75,000 square feet of space for labs, classrooms, and administrative offices. Scientists from Duke will be encouraged to conduct research at the new medical school, as well as to collaborate with academic and private research groups at Biopolis.

SPACE UPDATES ON RESEARCH DRIVE

- **The Global Health Research Building** (GHRB), which houses research and administrative space for the Southeast Regional Center of Excellence for Emerging Infections and Biodefense, was finished this winter.
- Renovations for Cell Biology in the **Nanaline Duke Lab** are in progress. An area of the Nanaline Duke Lab that was damaged in September by a fire has been prioritized for renovation.

ALSO ON THE NEW BUILDING SCENE

- The new **Duke Integrative Medicine** building was dedicated in November.

- The Duke Medicine Plaza office building opened on the campus of **Duke Raleigh Hospital**—the first step of a master plan initiative for Duke Raleigh.

- **Durham Regional Hospital** continues its renovations, including new flooring, exterior painting, and the addition of a new emergency generator.

Reading genes like tea leaves

FOR THE FIRST TIME, doctors who treat cancer patients may be able to determine early on which treatments will give each individual the best results. Scientists at Duke's Institute for Genome Sciences & Policy have developed a panel of genomic tests that analyzes the unique molecular traits of a cancerous tumor and determines which chemotherapy will most aggressively attack that patient's cancer.

In the November 2006 *Nature Medicine*, the research team led by Joe Nevins, PhD, and Anil Potti, MD, report 80 percent accuracy in their experiments, which applied these genomic tests to cells derived from tumors of cancer patients. The tests scan thousands of genes in the patient's tumor to produce a genomic profile of the tumor's molecular makeup. Using this profile to match a tumor to an effective chemotherapy could replace the current trial-and-error approach, which often requires patients to undergo multiple toxic therapies.

The first clinical trial of the tests will compare how well patients respond to chemotherapy when it is guided by the new genomic predictors versus when it is selected by physicians in the usual manner. Researchers plan to enroll about 120 patients with breast cancer in the first trial, with hundreds more patients who have lung and ovarian cancers in subsequent trials. If proven effective, says Nevins, this research will lead to more efficient use of the drugs physicians already have available in standard practice. "The tests simply provide an approach to better selection within our existing repertoire," he says, which spares patients the physical and emotional tolls of multiple failed strategies.

"Chemotherapy will likely continue to be the backbone of many anticancer treatment strategies," says Potti. "With the new test, we think that physicians will be able to personalize chemotherapy in a way that should improve outcomes."

A GENETIC ROADMAP FOR LUNG CANCER

Lung cancer kills more Americans each year than breast, prostate, and colorectal cancers combined. But chemotherapy is so toxic that the drugs are currently prescribed only to patients with large and aggressive tumors. Patients with early-stage lung cancers typically receive only surgery—even though chemotherapy could be lifesaving for the 30 to 40 percent of early-stage patients who will experience recurrent tumors, which are usually fatal. Unfortunately, physicians simply had no reliable way to tell which early-stage patients were at risk—until now.

In 2007, Duke will begin a landmark multicenter clinical trial of the first-ever genomic test to indicate which patients with early-stage, non-small-cell lung cancer should receive chemotherapy. According to findings published in the August 10, 2006 *New England Journal of Medicine*, the Lung Metagene Predictor test, developed by researchers at the Duke Institute for Genome Sciences & Policy, can identify patterns of gene activity in individual tumors to predict with up to 90 percent accuracy whether a patient is likely to suffer a recurrence, and should therefore receive aggressive treatment with chemotherapy. By providing the critical information needed to guide such treatment decisions, the test could save thousands of lives each year, investigators say.

Learn more at www.genome.duke.edu/lung_cancer/form.html.

A new hook and jab to fight kidney cancer

BY USING A NEW combination of two drugs, Duke researchers have dramatically improved response rates of patients with metastatic kidney cancer, which is generally considered incurable. The drug combo is not a cure, but it may slow disease progression in significant numbers of patients.

In the study, 40 percent of patients who received the newly approved drug sorafenib (Nexavar) along with the established drug interferon-alpha experienced "major shrinkage" of all their tumors—generally defined as 30 percent or greater shrinkage of all tumors in the body. In comparison, only 5 percent of patients who receive sorafenib alone show a major response, and just 5 to 10 percent of patients show a major response to interferon-alpha.

"By combining the drugs, we are seeing more major responses in greater numbers of patients, but we don't yet know how long the responses will last," says Duke's Jared Gollob, MD, who presented the findings at the 2006 annual meeting of the American Society of Clinical Oncology. "There are great new drugs on the market with relatively low toxicity, but the question physicians now face is how to make them work better for patients."

To learn about participating in the study, call 919-620-5354.

Proving the power of RNA

ACTING AS A GENETIC Trojan horse, a new RNA-based drug—the first of its kind—may prove a powerful tool against prostate cancer. In tests in mice with prostate cancer, the drug shrank the size of their tumors by half, and the mice showed no side effects from the treatment.

The experimental drug tricks its way into prostate cancer cells and then springs into action to destroy them, while leaving normal cells unharmed. The drug uses one type of genetic material, called an RNA aptamer, to attach to a protein, PMSA, found only on the surface of prostate cancer cells. When that module binds to a cancer cell, the cell reacts by engulfing the entire drug molecule. Once inside the cancer cell, a second module containing silencing RNA launches its effect. The silencing RNA seeks out and binds to the cancer cell's RNA for a cell-survival protein, called PLK1, and tags it for destruction.

"This study represents the first step in creating an RNA-based drug for cancer," says lead author James McNamara, PhD. He cautions that much work remains to move the experimental drug into clinical use, but says this study, reported in the August *Nature Biotechnology,* "provides a 'proof of principle' that an entirely RNA-based drug can work with minimal side effects."

Some like it hot: HIFU for prostate cancer

A SHOWDOWN between high heat and deep freeze may lead to a new therapeutic option for prostate-cancer patients. A multi-center national trial, with Duke as a lead participant, is comparing the effectiveness of cryotherapy, an established, popular treatment for prostate cancer, with a novel procedure called HIFU, or high-intensity focused ultrasound. HIFU, a technique used in Europe since 1993 and currently available in Canada, Mexico, and other U.S. neighbors, has yet to be approved by the Food and Drug Administration (FDA).

Duke urologic surgeon Cary Robertson, MD, is leading the study at Duke. He says that HIFU could be the next prostate-cancer treatment "darling," because it offers effectiveness comparable to traditional treatment modes without surgery or radiation. Like cryotherapy, HIFU has a low risk of post-procedure incontinence; it also offers a lower risk of erectile dysfunction than cryotherapy, Robertson says.

Robertson notes that this procedure is intended for men with small tumors and small prostates, which is about 20 percent of prostate-cancer cases. Many men with this profile are currently receiving radioactive seed therapy, in which tiny radioactive seeds are implanted into the prostate to destroy prostate tissue with minimal damage to surrounding nerves and muscles. But HIFU may do seeds one better, by offering a reduced incidence of incontinence, irritation, and erectile dysfunction.

> "Googling" American patients are asking about high-intensity focused ultrasound, which has been used to treat prostate cancer in Europe since 1993.

Because HIFU is sometimes associated with post-procedure swelling of the prostate, Robertson says his patients do have a catheter for about 10 days after the procedure. But he notes that, at least in his arm of the trial, none of his patients have had problems with incontinence, and the youngest of his patients reported no problems with erectile dysfunction—a side effect that occurs about in about half the patients, mostly older men, who receive HIFU in Europe.

Cary Robertson, MD

Robertson says that many "Googling" American patients are requesting the procedure, and some travel to Canada and Mexico to get it. In fact, there is currently a smattering of U.S. surgeons—trained by a urologist in Miami—who fly with groups of patients to Mexico in order to provide HIFU in a country that allows it. Robertson says this is a signal that the United States needs to make a firm decision about its own recommendations. "This procedure is on our borders," he says. "Duke needs to be at the forefront of testing its efficacy."

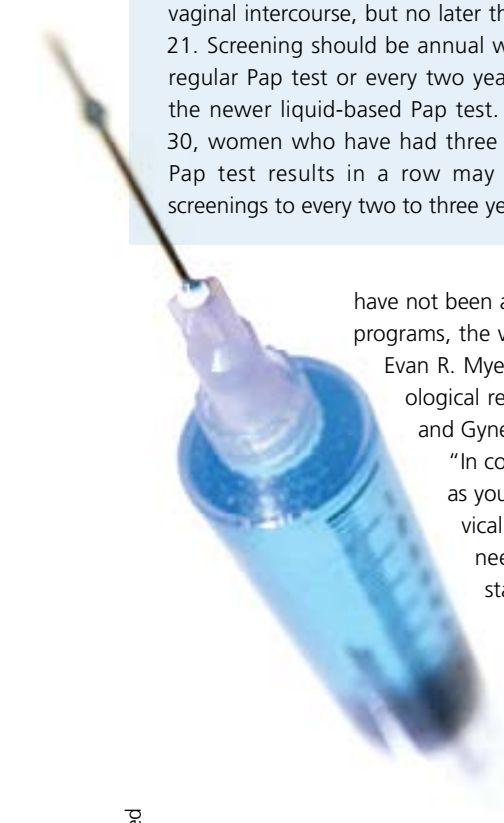
For more information on the trial, call Jill Smith at 919-668-3613.

A shot in the arm for cancer prevention

POTENTIAL CONTROVERSY over vaccinating girls against the sexually transmitted human papillomavirus (HPV) simmered in the media for months, but never quite came to a boil. The vaccine's demonstrated efficacy in preventing cervical cancer and genital warts caused by HPV ultimately outflanked concerns that its availability might encourage sexual activity; in June, to more fanfare than uproar, the FDA approved the vaccine Gardasil.

The Upshot: HPV Vaccination and Screening

- The vaccine Gardasil is recommended for females ages 11 to 26 and deemed safe for girls as young as nine.
- Vaccination is most effective before the onset of sexual activity, but is recommended regardless of sexual history.
- Until more data are available about the vaccine's duration, current Pap test recommendations are still in place. American Cancer Society guidelines suggest women begin cervical cancer screening about three years after they begin having vaginal intercourse, but no later than age 21. Screening should be annual with the regular Pap test or every two years with the newer liquid-based Pap test. At age 30, women who have had three normal Pap test results in a row may reduce screenings to every two to three years.



Gardasil is highly effective against four strains of HPV, including types 16 and 18 that are responsible for about 70 percent of cervical cancers. (Cervarix, which also targets types 16 and 18, is expected to hit the market in 2007.) The Centers for Disease Control (CDC) now recommends that the HPV vaccine be routinely given to girls 11 to 12 years old, and on the strength of the CDC endorsement Medicaid and many insurance companies are covering the cost.

The introduction of the vaccine has big implications for national and world health. "In developing countries that have not been able to implement cervical cancer screening programs, the vaccine really provides an alternative," says Evan R. Myers, MD, MPH, chief of clinical and epidemiological research in Duke's Department of Obstetrics and Gynecology.

"In countries that already have screening in place, as you reduce the incidence of precancer and cervical cancer through vaccination, you shouldn't need to screen as often and may be able to start screening at a later age."

REDUCED NEED FOR SCREENING

Reducing screening is important from a cost perspective, but it's also "a quality of life issue," according to Shalini Kulasingam, PhD, research associate in obstetrics and gynecology and senior fellow at Duke's Center for Clinical Health Policy Research. "With screening you have a lot of opportunities to have the disease detected at a precancer stage and treated. However, studies show that having an abnormal Pap smear can be stressful for women." In addition to the patient's emotional distress, she points to growing evidence that some of the treatments for high-grade precancer may increase a woman's risk of preterm birth via premature rupture of membranes.

Because we screen frequently in the U.S., and because it's not known which cases of cervical precancer, or dysplasia, will go away and which will develop into cancer, a lot of women may be getting treatment they don't need. "Very few women infected with HPV go on to develop any abnormalities at all," says Myers, "and most who do never develop cancer."

Myers and Kulasingam, who co-authored a 2003 study assessing the cost-effectiveness of HPV screening program strategies, expect that ultimately an effective vaccine will enable women to screen less frequently and perhaps delay their initial screening. "Every model we've looked at so far consistently indicates we should be able to reduce screenings and have the same or even better outcomes at lower cost with the vaccine," says Myers. "But until there are longer term data about length of protection, there won't be any major shifts."

GOOD FOR THE GANDER?

While the vaccine is not currently approved for use in males, that possibility is being explored. FDA and CDC sought safety data on males, and Merck is doing an efficacy study. "Because you need both men and women to transmit the disease, you could potentially reach herd immunity faster," says Myers. "But there may be ethical issues in vaccinating one population solely for the benefit of another. However, Gardasil protects against the strain of HPV that causes genital warts, and that's of direct benefit to men."

The vaccine's effectiveness in men will be harder to demonstrate because, as Myers observes, "Men don't get Pap smears."

Big-hearted mice: The good, the bad, and the gorgeous

MARATHON RUNNERS and hypertensive couch potatoes share some unusual physiology: both are apt to have enlarged hearts, created by cardiac overload. Why are some overgrown hearts a sign of cardiac health, while others indicate a risk for heart disease?

Researchers' best guess has been that duration of cardiac stress was key to determining risk: Exercisers burden their hearts for short periods, while hypertensive hearts beat under a constant strain. But a new study published in the June 2006 *Journal of Clinical Investigation* shows that heart enlargement itself actually has little to do with predicting disease. Instead, the nature of the physiological stress—and the molecular changes in heart cells that the stress may cause—is what matters.

Duke cardiologist Howard Rockman, MD, led a team of Duke and University of North Carolina-Chapel Hill researchers who occluded the aortas in a group of mice for 90 minutes twice a day. A second group of mice exercised for 90 minutes twice a day, either by swimming or running in a wheel. "After seven days, the hearts of the swimming mice were gorgeous," says Rockman. The hearts of the hypertensive mice were similarly enlarged and appeared from the outside to be functioning normally, but detailed genetic and histological analyses of the hearts and cardiovascular systems of all the mice showed significant structural and cellular abnormalities in those with blocked arteries. The studies also showed that these potentially harmful responses can begin even before the heart itself begins to enlarge.

The brain's symphony of scent

DUKE RESEARCHERS have discovered how the brain turns a hundred volatile chemical compounds assaulting the nose into the perfume of a rose.

In research published in the June 16 *Neuron*, researchers analyzed scents as diverse as peanut butter, coffee, and fresh bobcat urine, separating and identifying the volatile compounds in each odor with gas chromatography. "A complex mixture like urine has at least a hundred separate compounds in it," explains neurobiologist Da Yu Lin, PhD, who conducted the research as a graduate student studying with the late Lawrence Katz, PhD, a Howard Hughes Medical Institute investigator at Duke.

The team then exposed mice to the original odor and its individual compounds, and used a sensitive camera to map the responses of neurons across the olfactory bulb. "We found that glomeruli, the functional units of the olfactory bulb, act as detectors for individual compounds," says Lin. "There are no single detectors for complete smells." So to distinguish different scents, researchers speculate that the bulb likely passes the data to more advanced brain structures, where it is assembled and recognized as an odor. According to the researchers, it's as if the brain has to listen to each musician's melody to hear the full symphony. In terms of smell, says Lin, "The whole really is the sum of its parts."

, Duke-style

have known which cells in our tongues are the ones that detect tastes that ter, sweet, and umami (the taste Americans associate with MSG). A team y Duke researchers recently added sour to that list, by identifying two sour- ecting proteins in the taste buds.

Lead researcher Hiroaki Matsunami, PhD, says that identification of these oteins—PKD1L3 and PKD2L1—could lead to ways to manipulate the percep- on of taste, in order to fool the mouth that something sour, such as some ildren's medicines or health foods, tastes sweet. It also could lead to a better derstanding of how the sense of taste functions neurologically. "We still do know what is happening," says Matsunami, "in terms of exactly how the interprets the signals coming from the tongue to tell the difference between and lemonade." Findings appear the August 15, 2006 *Proceedings of the cademy of Sciences*.

Finally, a comeback against staph

STAPHYLOCOCCUS AUREUS bacteria, a leading culprit in bloodstream and surgical site infections, now causes up to 2 million infections and 90,000 deaths per year worldwide—most of them in health-care settings. For the last two decades, there have been no new drugs to stymie its progress. But a new international clinical trial led by Duke researchers has prompted the FDA to approve the drug daptomycin for treating heart infections and bacteremia, also known as bloodstream infection or blood poisoning, caused by *S. aureus*.

Duke infectious disease specialist Vance G. Fowler Jr., MD, participated in the study, published in the August 17 *New England Journal of Medicine*. "This advance adds a new weapon to our dwindling arsenal of antibiotics against these difficult-to-treat infections," he says—dwindling because many strains have developed resistance to all penicillin-related antibiotics. For these highly resistant strains—called methicillin-resistant *S. aureus*, or MRSA—the drug vancomycin has been the only consistently reliable treatment alternative. And recently MRSA strains resistant to vancomycin have appeared.

Daptomycin had already been approved by the FDA in 2003 for treating skin infections caused by *S. aureus*. But until now, Fowler says, no one knew definitively whether the drug would be effective against the more serious bloodstream and heart infections. "Having another drug in our armamentarium against *S. aureus* not only will give physicians a new treatment option, but also may help slow the current troubling spread of drug resistance among these bacteria," Fowler says.

A wonder drug gets more wonderful

REGULAR TREATMENT with the statin drug atorvastatin (Lipitor) soon after a stroke can reduce the risk of recurrent stroke by 16 percent in people who have no known history of coronary heart disease. This is according to an international, five-year study called the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial.

The study, published in the August 10 *New England Journal of Medicine*, is the first to document this new use for statin drugs, which lower levels of LDL cholesterol. Larry B. Goldstein, MD, director of the Duke Stroke Center and a member of the SPARCL steering committee, says that the findings will have a major effect on how people are treated following a stroke. "It's an important study because it shows that the addition of this drug to other treatments further reduces the risk of another stroke, which is a pretty big step in improving what we can do for stroke patients."

Atorvastatin confers an overall protective effect: In addition to reducing recurrent stroke risk, it can also reduce stroke patients' risk of heart attack and other major coronary events by 35 percent.

The drug also seems to be effective in patients who suffer a transient ischemic attack, or mini-stroke, which is considered a warning sign or prelude for stroke. According to this study, atorvastatin confers an overall protective effect: In addition to reducing recurrent stroke risk, it can also reduce stroke patients' risk of heart attack and other major coronary events by 35 percent; their risk of cardiovascular events such as unstable angina by 42 percent; and their need for coronary revascularization procedures, such as bypass surgery or cardiac catheterization, by 45 percent.

Whom to staple and whom to skip

HERE'S A TESTAMENT to the flourishing obesity epidemic: in 2005, roughly 170,000 Americans underwent gastric bypass surgery. The surgery helps people who are morbidly obese lose weight by stapling off a large portion of the stomach and reattaching the intestine to the smaller remaining portion. The resulting weight reduction will save the lives of many of these patients; but, as with any type of surgical procedure, gastric bypass surgery carries a risk of adverse side effects or even death. The key to optimizing safety, says Eric DeMaria, MD, director of bariatric surgery at Duke, is determining which patients are at the lowest risk.

Duke surgeons have developed a simple scoring system that can predict which candidates for gastric bypass surgery are at highest risk for dying. After analyzing the outcomes of all 2,075 patients who underwent the procedure between 1995 and 2004 at Virginia Commonwealth University (where DeMaria formerly practiced), the researchers identified five factors that were independently predictive of increased risk: a body mass index of greater than 50, male gender, hypertension, pulmonary embolus risk, and increased age.

If validated by additional studies, the new scoring system not only would give surgeons concrete information on which to base treatment options, but also would help patients make informed decisions about potential risks. The scoring system could also provide a standardized way to compare outcomes among centers that perform the surgery.

Better breast reconstruction

DUKE IS THE only institution in North Carolina offering a specialized microsurgery technique for improved breast reconstruction after surgery to remove cancerous tissue. Called DIEP (pronounced "deep") flap surgery, the procedure uses fat and skin tissue from the abdomen to create a breast that looks and feels natural.

Unlike the current standard, transverse rectus-abdominus muscle [TRAM] flap surgery, the DIEP procedure avoids sacrificing muscle tissue to construct the breast. In this way it offers a reduced recovery time, minimal scarring and muscle weakness, and fewer complications than its predecessor. Patients usually resume all their normal activities within three to four weeks.

Duke plastic surgeon Michael R. Zenn, MD, says the surgery is "a wonderful option for many patients, because it gives them a breast that will age naturally and the process itself causes far fewer medical problems than other reconstructive methods."

Not all women are good candidates for DIEP flap surgery. Patients must be free of medical problems, especially heart or lung disease or conditions related to obesity, Zenn says. Most importantly, patients must have enough fat and skin tissue to create a breast mound.

For more information, visit plastic.surgery.duke.edu.

Gastric bypass expertise

The Duke Weight Loss Surgery Center at Durham Regional Hospital has been named an American Society for Bariatric Surgery (ASBS) Center of Excellence. The designation recognizes surgical programs with a demonstrated track record of favorable outcomes in bariatric surgery, and these programs share information on clinical pathways, protocols, and outcomes data.

Under the knife—and better off

PEOPLE WITH SEVERE CORONARY artery disease live significantly longer if they receive bypass surgery as their initial treatment instead of artery-opening angioplasty or heart medications, according to a Duke analysis of outcomes from over 18,000 heart patients.

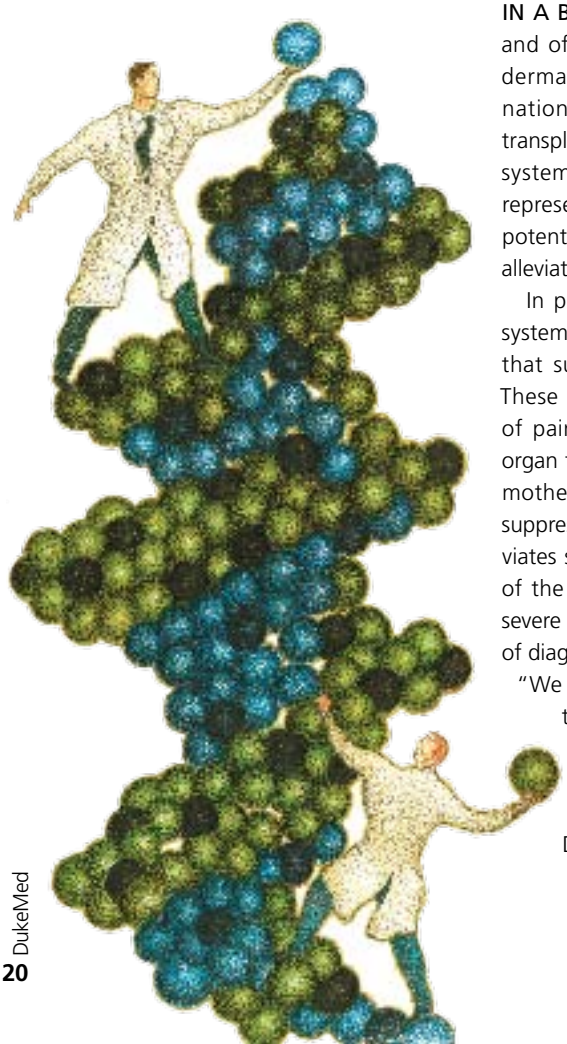
In a key part of the study, the researchers examined outcomes of patients with severe disease treated between 1996 and 2000 (when stents, which significantly reduce rates of artery reblockage after angioplasty, first came into widespread use). The patients who received bypass surgery lived an average of 5.3 months longer than those treated by angioplasty. In other study results, the researchers found that both bypass surgery and angioplasty provided more benefit for patients than medicines alone.

Yet the researchers estimate that up to 40 percent of patients diagnosed with severe coronary disease are treated first with angioplasty or medications and not given the opportunity to receive bypass surgery. "These findings should change practice," says lead investigator Peter Smith, MD, chief of cardiothoracic surgery. "It may sound very appealing to patients with severe coronary artery disease to get a treatment that is less expensive or less invasive, but they may not be getting the same survival benefit as patients receiving bypass surgery."

Smith notes that, while the study period ended before the widespread use of "drug-eluting stents," which slowly release drugs to keep the treated artery open, "We believe that our findings have a particular relevance to practice today, since recent studies suggest that there may be problems with the long-term durability of drug-eluting stents."

Study results were reported in the October 2006 *Annals of Thoracic Surgery*.

Scleroderma: Can stem cell transplants help?



IN A BOLD attempt to control the disabling and often fatal autoimmune disease scleroderma, physicians at Duke are leading a national study to test whether stem cell transplants can reconstruct defective immune systems. If successful, the therapy would represent the first therapy ever to treat and potentially reverse the disease itself, not just alleviate its symptoms.

In people with scleroderma, the immune system attacks the body's connective tissues that support the skin and internal organs. These patients experience varying degrees of pain, inflammation, hardened skin, and organ failure. The standard therapy is the chemotherapy drug cyclophosphamide, which suppresses the immune system. The drug alleviates symptoms but doesn't alter the course of the disease—about half of patients with severe organ involvement die within five years of diagnosis, despite treatment.

"We are hoping that stem cell transplantation will actually lessen or eradicate the defective immune response that initiates and perpetuates the disease," says Keith Sullivan, MD, a Duke oncologist and the lead investigator for the seven-year, multi-site study called SCOT (Scleroderma Cyclophosphamide or Transplantation). SCOT will compare the effects of 12 monthly treatments with high-dose cyclophosphamide versus stem cell transplantation, which is traditionally used to cure aggressive and recurrent cancers or inborn errors of the immune system.

Scleroderma affects up to 100,000 Americans and strikes three to four times as many women as men. The SCOT study is being funded by a $20-million grant from the National Institute of Allergy and Infectious Diseases; it will enroll 226 patients at 36 institutions nationwide.

For more information, including a list of participating sites, visit sclerodermatrial.org or call the hotline at 866-909-SCOT.

A closer look at pregnancy-related deaths


Haywood L. Brown, MD

A SWELLING BELLY and midnight pickle cravings are among the obvious symptoms of pregnancy, but Haywood L. Brown, MD, chair of Duke's Department of Obstetrics and Gynecology, wants physicians to remember that some symptoms indicate serious problems.

Pregnancy-related deaths have plummeted in the last century, but the overall mortality rate of women who are pregnant is climbing because of trauma and other deaths not related to the woman's health, says Brown. Today, the leading cause of non-pregnancy-related deaths among white women is motor-vehicle accident; for black women, it is homicide.

In North Carolina, 108 women died between 1995 and 1999 due to complications from pregnancy. That number is small when compared with the mortality rates of 50 or 75 years ago, but it still includes pregnancy-related deaths that researchers consider preventable. The deaths are also unevenly distributed, with black women bearing the brunt of the risk.

According to results of a statewide review by the North Carolina Pregnancy-Related Mortality Review Committee (published in *Obstetrics & Gynecology* in December 2005), the top causes of pregnancy-related death were hemorrhage, amniotic fluid embolism, cardiomyopathy, and complications from chronic illnesses such as heart disease, hypertension, and diabetes. Forty percent were ruled preventable. While deaths due to amniotic fluid embolus, microangiopathic hemolytic syndrome, and cerebrovascular accident were ruled unpreventable, the panel found that almost all hemorrhagic deaths and deaths from complications of chronic illnesses were potentially preventable.

"We felt these deaths resulted from problems in the health system or in access to care," says Brown, who served on the committee. "For example, perhaps a woman with severe heart disease was not made aware that pregnancy was a serious health risk for her. Or a woman didn't have the resources for prenatal care and developed fatal hypertension. Also, if there was a lack of planning for follow-up or transfer of care and it led to the patient receiving suboptimal treatment at any point, we consider those preventable deaths."

The committee noted with concern that 46 percent of the deaths among African American women were potentially preventable, while only 33 percent of the deaths in white women were preventable. The disparity may be explained in part by the higher incidence among black women of hypertension, heart disease, and type 2 diabetes. "We need to reinforce prenatal counseling for these women," says Brown. "We want to make sure that if a woman at significant health risk chooses to undertake a pregnancy, she does so with a full knowledge of the risks.

"There hasn't been a significant decline in pregnancy-related deaths since 1982," Brown adds. "That's part of what compelled us to do this study. We want to know what the system issues are, what the preconception issues are, what the diagnostic and treatment issues are that we could be working on to reduce that rate and understand the disparity in mortality." He was surprised, for example, by how often deaths from ectopic (tubal) pregnancies still occur—sometimes because a woman with subtle symptoms is misdiagnosed.

"While we are talking about 'only' four to eight deaths per hundred thousand pregnancies, if it's our daughters, sisters, or wives we're talking about, then that small number takes on a profound significance."

the making of a mirac

HOW ONE DUKE SCIENTIST'S PASSION INFUSED A MEDICAL CENTER, TRANSLATING—15 YEARS, MILLIONS OF DOLLARS, AND HUNDREDS OF HELPING HANDS LATER—INTO A LIFESAVING TREATMENT FOR A GENETIC DISORDER THAT ONCE KILLED EVERY BABY IT TOUCHED

Jean and Mitch Kelly lost their son Ryan to Pompe disease in 1995. Because the disease is an inherited genetic disorder, the couple—who also have a healthy son named Austen, now 14—decided not to have any more children. But then Jean became pregnant again. Amniocentesis showed that their third child indeed would be born with Pompe.

"It was horrible," says Jean Kelly. "I was five months pregnant. They called me at work with the results, and I went into the bathroom and I was just so angry. I was kicking the bathroom stall and crying, thinking this just cannot happen again. I don't think I can go through this again, I just can't lose another child. And then I felt the baby move."

By the time Jean arrived home that day her husband was at their computer, e-mailing pediatric geneticist Y.T. Chen, MD, PhD, at Duke. The couple had visited Chen five years earlier, when Ryan was diagnosed, and they knew Chen's team hoped to eventually launch clinical trials for a potential treatment. If the Kellys were very, very lucky, the couple thought, perhaps their youngest son could—unlike all other babies born with Pompe disease to that point—have a fighting chance at life.

BY MARSHA GREEN AND KATHLEEN YOUNT

THE TROUBLE WITH ENZYMES

The story of Myozyme—the first-ever treatment for Pompe disease, approved by the FDA just this spring—is one of awe-inspiring success. Like many such stories, though, it begins with a tragedy—and the consuming desire to never let it happen again. This is how Y.T. Chen describes his career spent fighting Pompe disease (pronounced "pom-PAY"), a glycogen storage disorder. The very rare disease results from what is essentially bad genetic luck—mutations on the gene that triggers the production of the enzyme alpha-glucosidase (GAA). Our bodies need GAA to break down the complex sugar glycogen for conversion into energy. If production of this enzyme is disrupted, glycogen builds up in the body's cells, damaging tissues and causing progressive muscle weakness.

For those born with infantile-onset Pompe, the disease progresses quickly. Increasing muscle weakness that is first noticed as a sort of "floppiness" and head lag leads to problems with swallowing and feeding; more critical, the heart muscle becomes thick and enlarged, and the baby develops respiratory problems. All babies with untreated Pompe disease die, most from cardiorespiratory failure, usually before their first birthday.

There is also an adult-onset form of the disease, and its progression can be slower and less severe. Ultimately this form of Pompe is also fatal, but since it can develop anywhere from childhood to late adulthood (patients have been diagnosed in their sixties), longevity is more varied.

Researchers like Chen have long sought a way to correct for these kinds of genetic mutations, set right the body's metabolic balance, and give life back to babies whose parents were often told by doctors to simply take them home and enjoy the time they had left. "When you look at Pompe babies, they are so helpless and weak, but they are so bright," says Chen, gesturing to his eyes. "They understand. The baby is asking you to help, and you just have to do something."

Chen has studied glycogen storage diseases since 1979, but he says in 1990 one infant in particular focused his sights on Pompe disease. The baby's family was seeking treatment at Duke, and Chen and his team hoped a bone-marrow transplant could help. It was going to cost a hefty $250,000; the family's community rallied to help raise the overwhelming sum. Then, before the transplant could even take place, the baby died.

Chen and a colleague went to Greensboro, North Carolina, to attend the funeral. Chen says the minister's eulogy changed his career. "He said, 'God, you gave life to a little angel, yet you took it away in such a short time. You must have had a purpose.' I looked at my colleague and we both knew, at that moment, that the purpose was for us to go back to the lab and find a cure."

need

"When you look at Pompe babies, they are so helpless and weak, but they are so bright. They understand. **The baby is asking you to help,** and you just have to do something."

—Y.T. CHEN, MD, PhD
pictured with Deeksha Bali, PhD

WHEN THE BIRD FLEW

The phrase "bench to bedside" is a friendly way to describe translational medicine, but seems almost too breezy to capture the relentless dedication required by so many researchers, clinicians, and families in an effort as monumental as the development of Myozyme. "In 1991 I thought it would only be a few years before we had a treatment," says Chen. "It took us 15." He points out that 15 years is the average time it takes for a drug to get from bench to bedside—but it feels much longer when parents are waiting for help for their fragile, weakening babies.

By 1995 Chen's molecular genetics laboratory had engineered a line of cells that could overproduce the GAA enzyme Pompe patients were missing. They also established that the GAA produced by those cells worked in cultured cells from these patients. Chen says it took several tries to identify a model that could make GAA enzyme that would be taken up by humans. "We went from *E. coli* to yeast to insect cells to mammalian cells. We ended up using cells from the ovaries of Chinese hamsters."

From there the researchers moved to animal studies. In 1996 they conducted an experiment using Japanese quail that, like humans with Pompe disease, were missing the gene for the GAA enzyme. These birds were so weak that they couldn't fly—when placed on their backs, they couldn't even right themselves. But when Chen's team injected the birds with their hamster-produced GAA enzyme, the results astounded everyone. After seven injections over 18 days, the birds could flip from their backs onto their feet. One of the birds even flew.

In Chen's lab at that time was a young postdoc, Priya Kishnani, MD, who had joined the group because of her interest in glycogen storage diseases. But her true passion was translational medicine, and at the moment that quail's wings stretched wide, her career, like Chen's, took on a dogged and narrow focus: This success meant clinical trials would come next, and Kishnani would ultimately be the investigator to take the helm.

A TRIAL OF THREE

The flying quail experiment earned Duke FDA approval for a phase I/II clinical trial of recombinant-enzyme therapy for Pompe disease. A British-based Taiwanese company, Synpac, obtained licensing from Duke to manufacture enough clinical-grade enzyme to treat a human baby—but they could make enough for only three patients.

"We didn't know how much we would need, but we knew that if it worked, we had to keep giving the enzyme to these babies to keep them alive," says study coordinator Joanne Mackey, a nurse practitioner. "That created a lot of tension, because we had to accept the babies on a first-come, first-served basis. And there were more than three babies whose families were pleading to be included."

Among those families were the Kellys. "We had stayed in touch with Duke throughout my pregnancy," says Jean Kelly. "We found the first spot filled. Then the second spot filled. And we were just lucky enough, the timing was just right for Jason to qualify for the third spot." He, like the other babies, would get intravenous, in-hospital infusions of the enzyme replacement for three months, with a fourth month of outpatient treatment. He could start in September 1999.

Still, it wasn't an easy choice for the family, who lived in Iowa. Jean would have to live with Jason in Durham, while Mitch stayed to work and care for Austen, who was seven at that time. Knowing firsthand how the disease would progress if the treatment failed, the family was reluctant to separate. "If it didn't work, and he died before his first birthday, we would have spent so much of his time split apart," says Jean. "It was really a hard decision."

trial

"We were nervous about enrolling the third baby. But when he had been on the treatment for 10 to 12 weeks and was still getting better, **that's when we really began to hope** that we had something big."

—JOANNE MACKEY, NP

The other two families in the trial traveled to Duke from Tennessee and Illinois. "At the beginning of the trial, the first baby was doing really well," remembers Mackey. "He was getting stronger and almost sitting. But then he began to decline. The second baby followed almost the same pattern." The mutations that lead to Pompe disease come in many types—researchers have identified more than 150 so far. Chen and Kishnani speculate that enzyme-replacement therapy is less effective in patients who have certain kinds of mutation (those resulting in no protein). Though the hearts of these first two babies responded well to the treatment, eventually both children died.

"We were nervous about enrolling the third baby," says Mackey, referring to Jason. But, she says, it was clear early on that his response to the infusions was going to be different. "When he had been on the treatment for 10 to 12 weeks and was still getting better, that's when we really began to hope that we had something big." That big thing was a big step—toward the development of a drug named Myozyme.

BREWING UP A TREATMENT

On the banks of the Charles River, just between the cities of Boston and Cambridge, sits a pretty brick building with rows of bright, green-tinted windows. Somewhere inside that building large metal cylinders are churning quietly and constantly, stirring a broth of vitamins and molecular growth factors around ever-multiplying batches of cells. These cylinders, called bioreactors, look something like giant moonshine vats—albeit with more tubes and a much smoother polish. But what they're brewing is stronger than any spirit. What these machines are making is an enzymatic potion potent enough to saves lives.

Since 1998 Genzyme, a Cambridge-based biotech company that specializes in treatments and cures for confounding diseases, has been working on the problem of Pompe. Between 1998 and 2002 they purchased rights from three companies to cell lines that could potentially become viable therapies. One of those companies was Synpac, the previous licensor of the cell line developed in Chen's lab, from whom Genzyme licensed rights in 2001. Then the company conducted what they called the "mother of all experiments" to evaluate their four candidate cell types. Ultimately, a Chinese hamster ovary cell line—similar to Chen's but developed at Genzyme—showed the most promise in terms of manufacturing potential.

Bench to bedside: Jian Dai, laboratory research analyst for Y.T. Chen, MD, PhD; Chen confers with Deeksha Bali, PhD, and Dai in the lab; Priya Kishnani, MD, with patient Ryan Clark at a follow-up visit.

Manufacturing the drug would be no small task. "The program to develop Myozyme was the largest in our 25-year history," says Bo Piela, spokesperson for Genzyme. "Through 2005 we spent approximately $500 million and had several hundred employees working on it. We built two 2,000-liter bioreactors. And we're now adding manufacturing capacity in Europe to ensure that we can produce enough enzyme to treat all the patients who need it." This is because, though Myozyme may act like a cure in that it can give many patients nearly normal bodies, its effects are ephemeral. Patients must receive continuing intravenous infusions of the therapy—Jason Kelly, for example, now undergoes the four-hour infusion every other Saturday, at a medical center near his home. All Pompe patients will have similar needs, for their entire lives.

Deya Corzo, MD, medical director of the Myozyme program at Genzyme, explains that Myozyme was a unique challenge even for a company built on unique drug-making challenges. "Pompe is so different," she says. "Everyone was so stressed because these babies would die, quickly, if we didn't do something. But it was a huge undertaking to produce so much enzyme."

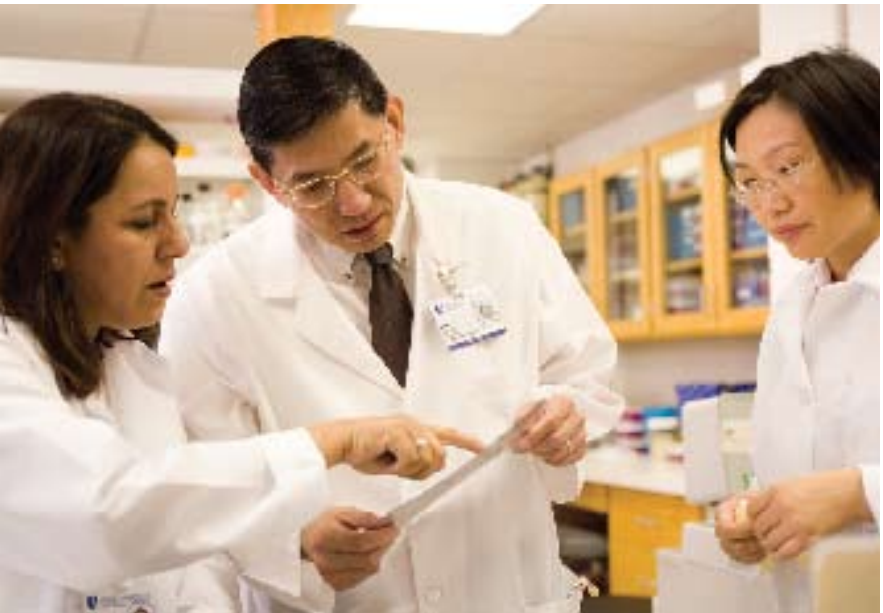
The cycle to grow Myozyme is three months; inside the huge bioreactors there are billions of cells producing the GAA enzyme, but every day scientists harvest only a bit of that fluid to carefully process it into what must be a frustratingly small amount of pure enzyme. And Corzo notes that Myozyme treatments require 20 times more drug than similar therapies developed at Genzyme. "The breakthrough came when our scientists were able to optimize the production of the enzyme," she says. "Only then could we think of doing larger clinical trials."

MAKING ROOM FOR MIRACLE BABIES

The trials were to continue at Duke, where a growing number of clinicians and study coordinators were fielding calls from families who, after the first trial was announced, simply started showing up. Genzyme and Duke launched a phase II trial in 2001 and a phase III trial in 2003, with Kishnani serving as Duke's principal investigator.

"There was always a sense of urgency to get the children signed up for the clinical trials," says Kishnani. "That takes a lot of effort. The consent form itself was 25 pages long, and there were always changes that needed to be made based on what we had learned from the babies already enrolled. When we ran into a rough spot and changed the protocol, we had to change the consent form, inform the families, and take it back to the institutional review board. (IRB chair) Dr. John Falletta worked very hard to ensure this was done in a timely fashion so that everything would be in place for the next child."

And the children kept coming, from all over the world. Genzyme reports that of the 40 families who participated in Myozyme clinical trials, all but one had to relocate, often from halfway around the world. One South African family, the Vaheds, took Duke by surprise when they arrived unannounced on the Fourth of July—they had been unable to obtain a medical visa and so traveled to Durham as tourists. "We'd take babies on Christmas Eve, Thanksgiving weekend," says Kishnani. Everyone knew that these children couldn't afford to wait on paperwork or national holidays—timely treatment with the enzyme was critical to give each baby the best chance of survival.





As each family arrived, Duke scrambled to help them settle in for what could be many, many months. "Genzyme representatives, Duke social workers, and others helped the families relocate to Durham by coordinating apartments and registering children for school," says Stephanie DeArmey, a Duke physician assistant and Pompe study coordinator. She says she and her colleagues became very attached to each uprooted family. "We were on page 24 hours a day for these families—not just for medical issues, but social issues as well. We spent a lot of time with the families and celebrated milestones such as birthdays for the kids."

Genzyme administered trials of Myozyme at seven sites in the United States, Europe, and Asia; Duke was the first and largest site. But there were also many children who were likely to benefit from Myozyme but who didn't meet the strict criteria for the trials or who came along after the clinical trials were full. So Genzyme got permission to launch an expanded access program, to provide Myozyme therapy to these patients before official FDA approval. Often these patients began their therapy at Duke, while Genzyme and Duke helped their local hospitals get set up to provide the infusions.

THE TESTING OF METTLE

Kishnani says that during the clinical trials, the team working on Pompe disease became more like a family. "Each and every person on the team has been so committed to this mission," she says. "I never heard 'no' from anyone. It was always, 'If I can't do it, I'll figure out who can.'"

It was an effort that ultimately required the whole Duke community to take a leap of faith. "It was not an easy road," Kishnani explains. "These babies were so sick, and our effort was experimental and so time-consuming." The trials needed anesthesiologists, cardiologists, pulmonologists, speech and language pathologists, social workers, physical and occupational therapists, nurses, physician assistants. "Everybody had to buy in," Kishnani says, including the Duke administrators who allowed more and more institutional resources for the trials. "If it wasn't for the goodwill of all these friends and colleagues at Duke, I don't believe we would have had the same success."

Mackey agrees that the clinical trials were not a clear-cut, easy path. "There were some very tough times," she says. She and Kishnani both speak of the first child enrolled in the clinical trial for babies six months or older. "We had been following her for a while," says Mackey, "waiting for the trial to get her enrolled. When the protocol was approved and she was finally enrolled, the first thing that was called for was a muscle biopsy, which required anesthesia. The baby died while in the operating room. It was devastating."

And, notes Kishnani, it rocked the whole trial on its heels. Part of the problem was the enlarged hearts of the Pompe babies, which grow weaker as the disease progresses. "These babies are so fragile when they come in—just turning them over in the crib can be a stress that changes their medical status," says pediatric physical therapist Laura Case, DPT, who joined the team in 1999.

The team regrouped, working with Duke anesthesiologist Richard Ing, MD, to create a protocol for safe delivery of anesthesia, and Duke and Genzyme revamped the consent form. As always, the team worked at top speed. "There were babies ready to be enrolled," says Kishnani, "but we couldn't take them until we had fixed the anesthesia issues."

"Over the years it has been amazing to watch how they fine-tune the treatment," adds Lynda Everett, a nurse on the Duke Clinical Research Center's Rankin Unit, where most of the Pompe patients received

A joyful reunion: Pictured at the August 2006 Pompe reunion at Duke are (from left) Jason Kelly, who as a baby participated in the first Myozyme trial, with his parents Mitch and Jean; Y.T. Chen, MD, PhD, with Haydee and Jorge Romero of Peru and their daughter Yamila; Abdurrahman Vahed, whose family traveled from South Africa to attend.

success

"I like to call it Duke at its best. But it's also industry at its best and it's also a marvelous statement about the courage of the patients and families." —R. SANDERS WILLIAMS, MD

their infusions. And as they learned and the trials wore on, one healthy baby became three, became eight, became two dozen and counting. Now, Everett says, "these kids are walking and talking. Sometimes patients come back to see us—that is amazing."

NO MAGIC, BUT A MODEL

With four years of clinical success behind it, Myozyme earned FDA approval for use in infants and adults in April 2006. The drug is now being used by over 500 patients in more than 50 medical centers across 20 countries. Patients can still vary significantly in their individual response to therapy, so more refinements will continue—a new clinical trial of Myozyme for adult-onset Pompe disease began in 2005 and is still under way.

As Genzyme continues to expand production, Duke personnel are training staff at Genzyme and other medical centers to administer Myozyme. "This drug can seem scary-looking," says Mackey. "It comes with a black-box warning about reactions and side effects. And it's not magic, it doesn't work overnight. It takes about eight infusions to see them get better, and there can occasionally be residual muscle weakness. We teach this to the families, to the nurses and others who are administering the drug. We're all teaching and learning from each other."

Genzyme's Deya Corzo calls Myozyme a model for partnerships between industry and academia. "There have been disagreements," she says, "but people always saw the bigger goal, and were optimistic that this product could change the course of this horrible disease."

This August Duke hosted a reunion, so that Pompe families and Duke and Genzyme investigators and administrators could gather to commemorate everything that led to Myozyme's approval. Kishnani spoke to the many lessons that the Pompe trials represented—lessons in humility, in the benefits of working as a team, and of the many different aspects of this disease. "They are lessons that have really made us better human beings," she said, "and lessons that I hope we can carry over to the treatment of other medically fragile children and infants."

"I like to call this Duke at its best," said R. Sanders Williams, MD, dean of the School of Medicine. "But it's also industry at its best and it's also a marvelous statement about the courage of the patients and families who participated in the clinical trials that proved Myozyme's efficacy."

At the reunion, Jason Kelly joined his mother at the podium to say hello to the guests and to thank Chen, Mackey, and the others who cared for him. Jean Kelly says that, though Jason has some slight muscle weakness—marathon running, for example, may not be his sport of choice—his disease is otherwise undetectable. The shy, towheaded, baseball-playing seven-year-old was all smiles—and maybe a look of mild puzzlement. "He was sort of wondering, 'What's the big deal?'" says Jean Kelly. "'Why does everybody want to take my picture?' We told him 'Well, you just aren't seeing what you mean to a lot of people.'" After all, she notes happily, he's just a normal kid, still too young to understand the enormousness of what his life represents.

The story of Myozyme is indeed enormous, a story of millions—millions of tiny cells multiplying, millions of hours and dollars invested, millions of tears shed in joy, sorrow, and frustration. And, as the father of one baby lost to Pompe disease pointed out, millions of stars in Durham's night sky, testaments to the babies whose short lives inspired the journey toward Myozyme. In memory of his brave young son, John—the first baby enrolled in the very first trial—Barry Koncel shared with those gathered at the reunion an excerpt from *The Little Prince*, which he and his wife used to read aloud to John: "Look at the stars and remember: In one of the stars I shall be living. In one of them I shall be laughing. And so it will be as if all the stars were laughing, when you look at the sky at night." □

The Long Hunt

Twenty-five years after the first AIDS diagnosis, scientists are taking research in new directions—with the goal of closing in on a vaccine at last.

BY DENNIS MEREDITH
ILLUSTRATION BY LEIGH WELLS

The white stucco buildings of the Chelstone Clinic in Zambia were meticulously clean, Barton Haynes saw on his visit. And the neatly dressed doctors and nurses were conscientious and caring in treating their patients. They efficiently ministered to a seemingly endless stream of people with AIDS and the host of other co-infections—like tuberculosis, fungal diseases, and cryptococcal meningitis—to which AIDS rendered them susceptible.

But it was the clinic's drug cabinets that betrayed the real emergency of AIDS in Africa.

"They were bare, except for painkillers like morphine," Haynes recalls of his 2001 visit. "Patients with AIDS and opportunistic infections could only be offered palliative regimens. The state-of-the-art drugs we have here were simply not available."

Haynes, an immunologist who was then chairman of the Department of Medicine at Duke, had gone to Zambia to enlist support for a research project to produce a combined HIV-tuberculosis-malaria vaccine. But that trip would change his life—by bringing him face-to-face with the appalling human tragedy of a country where nearly 20 percent of the population is infected.

"I saw the effect of AIDS in Africa on family structure and societal structure and in producing so many orphans. Virtually all Zambian families had lost family members to AIDS and were taking in the children who were left behind," he says. "And I saw that the gulf between what we have in the U.S., and what people living on a dollar a day have, was too great for our global society to be stable."

Until that trip, Haynes envisioned his

PHOTO COURTESY OF BARTON HAYNES

> [THE MEDICINE CABINETS] WERE BARE, EXCEPT FOR PAINKILLERS LIKE MORPHINE. PATIENTS WITH AIDS AND OPPORTUNISTIC INFECTIONS COULD ONLY BE OFFERED PALLIATIVE REGIMENS. THE STATE-OF-THE-ART DRUGS WE HAVE HERE WERE SIMPLY NOT AVAILABLE."
>
> *—Barton Haynes, MD, discussing his visit to Zambia in 2001*

future as that of a senior medical administrator. But the experience set him on a new path. "Rather than do some job that was so huge like chairing the department, where you were dealing with all of medicine, I decided to devote the last part of my career to developing vaccines for TB and HIV." After stepping down from the chairmanship in 2002, Haynes began to work full-time on global health issues, taking leading roles at both Duke's Human Vaccine Institute and the National Institutes of Health (NIH)-funded Southeast Regional Center of Excellence in Biodefense and Emerging Infections, or SERCEB, a virtual consortium of 21 universities dedicated to developing drugs, vaccines, and diagnostics against AIDS and other emerging infectious disease threats.

Ultimately, that pivotal trip to Africa and his own experiences as a scientist would lead Haynes to advocate for a brand-new approach to AIDS vaccine research—an approach realized last year with the launch of the Center for HIV/AIDS Vaccine Immunology (CHAVI). Based at Duke and led by Haynes, the $300-million global scientific consortium is one of the most ambitious efforts ever in the quest to develop an AIDS vaccine. By linking some of the world's best minds and most powerful scientific resources, CHAVI is expressly designed to give scientists the best possible chance of solving the AIDS puzzle at last.

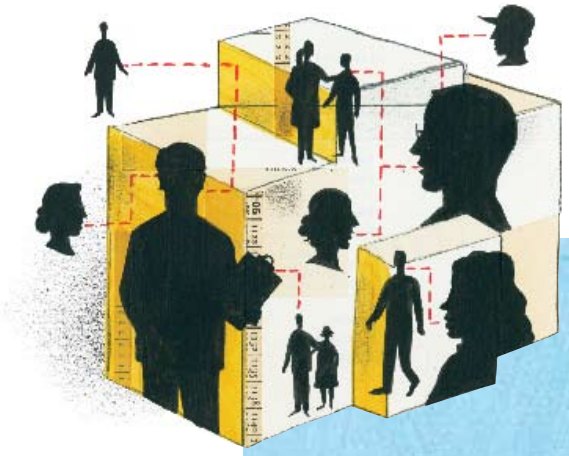
SNARES IN THE HUNT

The need for a better scientific offensive against AIDS was abundantly clear. A quarter-century after the first case of AIDS was diagnosed, the disease has become a global pandemic, growing exponentially worse with each passing year. Some 41 million people worldwide are now infected with HIV. The legions of infected could reach 100 million in a decade, and the total death toll could reach 70 million by 2020.

In the early years of AIDS, vaccine developers were wildly overoptimistic,

says Haynes. "We thought that this problem was going to be solved in two or three years. The group at Duke developed an envelope-based vaccine along the lines of the hepatitis B vaccine; we thought it was going to work, and then we'd move on to something else." (The viral envelope is the coat of proteins that cloak the virus; envelope-based vaccines present the body with slivers of that coat, in an effort to help the immune system recognize and attack the complete virus.)

As it turned out, the scientists had profoundly underestimated their enemy.



Fighting AIDS Together

WHEN ROYCE HARDIN first tested positive for HIV in 1990, he made his way to a cozy waiting room at Duke. There, he found not only treatment, but a family.

"There must have been about 50 people waiting, and lots of little kids playing in the corner, where there was a big basket of toys," recalls Hardin. "Back then, if someone was pretty far along with AIDS, you could certainly tell, and here I was newly diagnosed, looking around at white men, black men, white women, black women and thinking, 'Wow, this is amazing … all these different people can come together and understand something that the whole world needs to understand.' And then I met Dr. Bartlett and immediately knew that this man cared, he really cared."

The place was the Duke University AIDS Research and Treatment Center, or DART, and the physician was John Bartlett, MD, who has come to personify Duke's commitment to providing the very best treatment to AIDS patients. That treatment involves not only medical care, but providing a broad range of social and legal services patients may need. And it involves listening.

Recalls Hardin, "On my first visit to Dr. Bartlett, he just sat there listening and totally involved, even though at the time he had maybe 300 other patients. At the end of the visit he gave me a hug, and I told him how I think I acquired the virus. It was the first time I really let myself feel my sorrow about it."

Bartlett's philosophy of understanding and treating the whole patient has guided all who work at DART, says Hardin. "Their attitude is 'We are your family and we are going to take care of you.'"

Even as the AIDS epidemic has caused DART to grow to some 1,700 patients over its two-decade history, DART has continued its commitment not only to personalized patient care, but to advanced clinical trials, says Bartlett.

"Our objective is to foster a bi-directional flow of new treatments from laboratory bench to bedside, and of new research ideas from bedside back to bench," he says. Thus, DART has hosted a myriad of studies of antiretroviral drugs, vaccines, and combination treatments for co-infections of HIV and other diseases. And its research reaches far beyond the Duke clinic walls. A member of a NIAID-funded international clinical trials group, in collaboration with Kilimanjaro Christian Medical Centre in Tanzania, DART also works with CHAVI to recruit patients for basic studies to aid vaccine development, and has become a key player in Duke's new Global Health Initiative to reduce health disparities at home and worldwide.

"Ten or 15 years ago the prognosis was not especially good, but now to see so many of our patients thriving is deeply rewarding," says Bartlett. "I am especially pleased that a number of patients have achieved this longevity by participating in clinical trials that gave them access to new treatments that prolonged their lives.

"It gives me great joy to say that many of the patients that I take care of, I've taken care of for well over a decade," he adds. "And it is wonderful to grow old together."

For one thing, HIV is a moving target, easily mutating into new strains. The viral enzyme, reverse transcriptase, which copies its RNA genetic material into DNA when it infects a host, is conveniently error-prone. These continual genetic copying errors drive HIV's mutation rate to be some tenfold greater than that of another major global viral threat, influenza.

While many of these mutated strains die off in the survival of the fittest, others flourish, giving the virus new disguises it can use to hide from the immune system. The mutations alter the structure of proteins that constitute the viral envelope, thereby helping the virus evade recognition by the attack dogs of the immune system, neutralizing antibodies. Enhancing its disguise, the virus also enshrouds its coat proteins with sugar molecules that are invisible to the immune system.

Another secret of HIV's subversive success is that it targets the very immune system that seeks to destroy it, killing both "helper" and "killer" T cells to render the body vulnerable to fatal infection. Finally, the virus insinuates its genes into an infected cell's chromosomes, spawning a cadre of covert viral operatives that resist drug assault.

With such a slippery foe, "Everyone in the field got hit with some numbing defeats," recalls Haynes. "First was the realization that the antibodies that work for one isolate [a particular strain of HIV] don't work for others. We were beginning to see heterogeneity in the isolates, and that they were mutating and were enormously diverse. Then came the painful realization that the isolates we had all been using and growing in the lab were not relevant to the isolates being transmitted in the community. And the fact that the virus intercalates itself into the genetic material of the host is a huge problem that has yet to be solved."

Another central problem has been lack of basic knowledge of how the immune machinery responds to HIV, says Haynes. Traditionally, researchers simply produce a series of vaccines from weakened virus or various pieces of viral protein. They then test the candidates until the best one is found. However, says Haynes, for HIV none of the usual shot-in-the-dark approaches has worked. Currently, only two candidate vaccines—developed by Merck and the National Institute of Allergy and Infectious Diseases (NIAID)—are considered viable. And even these have modest goals, aiming only at lowering virus levels in infected people.

THE NECESSARY ADVANCE

There have been other advances in the field since 1981, of course—not least a raft of new drugs that can subdue the infection, effectively turning HIV/AIDS into a chronic disease (at least for those who can afford long-term treatment). Among those is the drug Fuzeon, discovered at Duke by Thomas Matthews, PhD. But the elusive vaccine remains critical to quelling the pandemic, assert public health experts. Even with the most far-reaching education and prevention programs and the most effective drugs, clinicians desperately need a vaccine to prevent AIDS or at least give the immune system a fighting chance to reduce levels of virus. As a recent NIH manifesto put it, "The ultimate defeat of HIV/AIDS . . . will be difficult, if not impossible, without a safe and effective HIV vaccine."

But it was clear the isolated research efforts of the past weren't getting scientists very far. In 2003, a seminal paper in *Science*—"The Need for a Global HIV Vaccine Enterprise"—called for a new tack to surmount past failures. Authored by Duke alumnus Richard Klausner, MD, Haynes, and some two dozen other prominent AIDS experts, the paper cited the lack of progress over the past two decades, and advocated a large-scale vaccine initiative that included establishing a coordinated global network of vaccine research, development, and testing centers.

That clarion call ultimately inspired the federal government to fund the initiative that would become CHAVI. Says Stuart Shapiro, MD, PhD, CHAVI program coordinator for NIAID, "We wanted a program that would enable a great deal of collaboration and be very transparent, enabling the AIDS research community [as a whole] to develop a vaccine. We didn't want just a small elite group working in one place, keeping all the information to themselves so that they would be the ones to develop a vaccine."

Haynes and his colleagues—drawing on their experience managing the virtual consortium of SERCEB—entered the CHAVI grant competition with a team of 36 institutions and 80 researchers. They won, and CHAVI was established in July 2005 with $15 million from NIAID. Over

BASED AT DUKE AND LED BY BARTON HAYNES, MD, THE $300-MILLION GLOBAL SCIENTIFIC CONSORTIUM KNOWN AS CHAVI IS ONE OF THE MOST AMBITIOUS EFFORTS EVER IN THE QUEST TO DEVELOP AN AIDS VACCINE.

its seven years of funding, it may receive more than $300 million. "CHAVI is an incredible blue-ribbon group," says Shapiro, "which is not to say there aren't other bright scientists in the field that we hope will contribute to its goals."

In July 2006, CHAVI received an extra infusion of support from the Bill & Melinda Gates Foundation as part of the foundation's $287-million Collaboration for AIDS Vaccine Discovery (CAVD). That program supports CHAVI and 15 other research consortia aimed at accelerating HIV vaccine development.

"We have all been frustrated by the slow pace of progress in HIV vaccine development, yet breakthroughs are achievable if we aggressively pursue scientific leads and work together in new ways," says José Esparza, MD, PhD, senior advisor on HIV vaccines for the Gates Foundation. "CHAVI is the first major initiative launched to support the global HIV vaccine enterprise, and it is showing how a large collaborative network can complement the creativity of individual investigators to accelerate the development of an HIV vaccine."

THE PROMISE OF NON-PROGRESSORS

As CHAVI gears up, its worldwide network of researchers is working to tackle some of the most difficult problems in HIV vaccine development.

A central mystery being explored by CHAVI scientists is why people infected with HIV show a spectrum of immune response. While some may quickly progress to AIDS, a rare few become "non-progressors," suppressing the virus so successfully that it remains undetectable in their blood.

Also intriguing is that a tiny percentage of people do not become infected in the first place, even though they apparently have been exposed to a heavy dose of the virus. Researchers cite as a classic example of such resistance members of a group of sex workers in Kenya, who did not become infected even after engaging in high-risk sexual behavior every day for years.

Haynes and other CHAVI researchers believe that somewhere in the molecular labyrinth of such people's immune systems could lie the key to a successful

Global Pandemic, Global Partnerships

"Duke's collaboration with our hospital has meant both greater research activity and new diagnostic machines and techniques that we didn't have before. It's enabling us to evaluate new treatments and to improve diagnosis and policy."

—Habib Ramadhani, Kilimanjaro Christian Medical Centre

JUST A FEW months ago, a young Tanzanian researcher—Habib Ramadhani of the Kilimanjaro Christian Medical Centre (KCMC)—traveled to the International AIDS Conference in Toronto to deliver results of a new study examining resistance to antiretroviral drugs. It was one of many new studies presented, but significant in that it was immediately applicable: The analysis revealed that patients who had to pay for drug therapy were more likely to skip their drugs, giving HIV a chance to proliferate and evolve resistance. The study supported a policy of providing such drugs free as critical to treatment adherence and thus to reducing spread of infection—findings that have the potential to influence HIV treatment not only in Tanzania, but around the world.

For Duke infectious diseases physician and medical microbiologist John Crump, MB, ChB, who works full-time at KCMC, the talk by his African colleague exemplified the success of Duke's long-standing collaboration with Tanzanian health centers. Duke has been fortunate, says Crump, to have developed close collaborations with two of Tanzania's leading HIV/AIDS research and health care organizations—KCMC and KIWAKKUKI, which focuses on HIV treatment and care and prevention. (KIWAKKUKI is the Swahili acronym for Women Fighting Vigorously Against AIDS in Kilimanjaro.) Among the most established of Duke's research and service partnerships worldwide, they are both inspiration for and an integral part of the university-wide Global Health Initiative, launched in April 2006 with the mission of reducing health disparities locally and worldwide.

While the Duke collaboration with KCMC focuses on HIV treatment and research, the partnership with KIWAKKUKI grapples with such issues as voluntary testing and HIV home-based care.

Clinicians and policymakers in both developed and resource-poor countries badly need each other's insights and knowledge to defeat the global AIDS pandemic, emphasizes Crump. For example, a study with KIWAKKUKI led by Duke's Nathan Thielman, MD, showed that free HIV testing greatly increased participation—a finding that could have policy implications not only locally, but worldwide.

Another study led by Thielman and Humphrey Shao, MD, focuses on the challenge of treating patients with HIV and active tuberculosis. "Patients newly diagnosed with HIV here in Tanzania often present with TB, and treating the two infections in parallel is a challenge," says Crump, pointing out that developed countries have little experience with co-infections of HIV and TB. "Clinicians must contend with the interactions between drugs for HIV and TB, and this study will help determine the best management approaches."

KCMC also participates in a NIAID-funded study led by John Bartlett, MD, among the largest ever to examine AIDS co-infections in developing nations. And in a study for CHAVI, researchers from Duke, the Harvard School of Public Health, and KCMC are seeking to identify and analyze the initial immune response of newly infected patients, research that could contribute to AIDS vaccine development.

Duke and KCMC also share an educational exchange program that offers both partners an opportunity to enhance their knowledge and train new workers—a signature goal of the Global Health Initiative. Some Duke medical residents spend three-month rotations at KCMC under the leadership of Ralph Corey, MD, of the Hubert-Yeargan Center for Global Health, and third-year medical students and fellows spend one or more years in Tanzania, helping them better understand how to work in resource-poor countries and contributing to joint research and service goals. And Ramadhani and a colleague have come to the U.S. to work on master's degrees in clinical research—taking their knowledge back to Tanzania to enhance research projects there.

Read more about Duke's partnerships in Tanzania and other work taking place through the Duke Global Health Initiative at globalhealth.duke.edu.

vaccine. For example, his own research, funded by the Gates Foundation, is tackling the mystery of why only very rare patients produce antibodies that keep the virus at bay. Intriguingly, the studies have revealed that the molecular structure of these antibodies resembles that of "auto-antibodies" that the body pathologically generates against itself in autoimmune diseases such as lupus.

"So, maybe these antibodies aren't normally made in infected patients because the body doesn't want to make them," says Haynes. "Maybe the virus is telling us, 'Yes, I have an Achilles' heel, but if you make an antibody to it, you will pay.'"

Haynes and colleagues are now seeking to develop a way to induce the body to create such antibodies without predisposing patients to autoimmune reaction—an effort that Esparza sees as highly promising. "The design of vaccines that can induce protective antibodies is probably the biggest challenge that the field is confronting, and Bart's project explores a totally new paradigm that can open new avenues for research," he says.

CHAVI's cadre of genetic researchers is also tackling the puzzle of non-progressors. For example, CHAVI researchers, who are performing comparative whole-genome analyses on thousands of people who have been exposed but not infected, are also planning a similar analysis among hundreds of infected people who show different abilities to control the virus in an international collaboration dubbed EuroCHAVI. The EuroCHAVI researchers will seek any distinguishing genetic characteristics of non-progressors (who control the virus the best) that could provide clues to vaccine development. EuroCHAVI is led by Duke's David Goldstein, PhD, and Amalio Telenti, MD, PhD, of the University of Lausanne, Switzerland. Similar studies are being performed in CHAVI in non-human primates by Norman Letvin, MD, of Harvard.

CHAVI researchers are also seeking to take advantage of the surprising discovery that only a relatively limited number

"THE CONCEPT WAS ALWAYS THAT TO CONTROL VIRUS YOU NEED A VERY PRONOUNCED IMMUNE RESPONSE. WELL, WE FOUND THE OPPOSITE," SAYS KENT WEINHOLD, PHD, WHO STUDIES THE RARE HIV-INFECTED INDIVIDUALS WHOSE DISEASE DOES NOT PROGRESS—EVEN WITHOUT TREATMENT—TO FIND CLUES THAT MAY HELP OTHERS.

> EVEN A GOOD PARTIAL IMMUNE RESPONSE MIGHT REDUCE VIRAL REPLICATION, LOWERING BLOOD LEVELS AND ENABLING THE PERSON TO REMAIN HEALTHIER. AND BECAUSE THEY DON'T HAVE MUCH VIRUS IN THEIR BLOOD THEY WOULD BE LESS LIKELY TO TRANSMIT."
>
> *—David Montefiori, PhD*

of the vast array of HIV strains are actually capable of being transmitted. By identifying those strains, University of Alabama at Birmingham scientists George Shaw, MD, PhD, and Beatrice Hahn, MD, hope to enable developers to greatly narrow the targets of their vaccines. And in an effort to find such strains, CHAVI researchers Myron Cohen, MD, and Joseph Eron, MD, of the University of North Carolina and Charles Hicks, MD, at Duke have organized a system for identifying North Carolina patients soon after the time of transmission, before their immune systems have had a chance to propel the virus into a frenzy of mutation.

STRENGTH IN NUMBERS

CHAVI's main scientific treasure trove—tens of thousands of blood samples from HIV-infected people—rests in a modest room of CHAVI's laboratories, ensconced in supercold freezers and liquid-nitrogen-cooled tanks. Continually gathered from around the world and genetically characterized, the growing collection of HIV strains perhaps best exemplifies CHAVI's international, collaborative character.

Duke's Kent Weinhold, PhD, and David Montefiori, PhD, along with Andrew McMichael of Oxford University in England, are helping to lead CHAVI's efforts to plumb this extraordinary collection to understand how HIV influences T cells and antibodies. The meticulously curated collection enables them and their colleagues to ask new scientific questions as research technology advances—for instance, using new analytical methods on the collection to trace how a non-progressor's infection evolved over time. From these studies, says Weinhold, have come crucial new insights into non-progressors' immune response. For example, he and his colleagues at the University of Maryland have gleaned important insights from their studies of two individuals—identified in a screen of 11,000 clinic attendees in Trinidad—whose disease did not progress.

"The concept was always that to control virus you need a very pronounced immune response," he says. "Well, we found the opposite. In these long-term non-progressors T-cell responses were HIV-specific, but by and large very low-level."

Weinhold and his colleagues are now continuing their studies to understand how the non-progressors' T cells achieve such specificity and potency. So far, the

studies have revealed that their T cells may be more "polyfunctional," able to mount multi-pronged molecular attacks on invading microbes.

"We can use this insight to develop vaccines that can induce the kinds of polyfunctional responses we see in these long-term non-progressors," says Weinhold.

Meanwhile, Montefiori and his colleagues have launched an effort to standardize and improve laboratory tests used to assess such new vaccine candidates. As part of the Gates Foundation-supported CAVD, Montefiori's laboratory is leading an international network of laboratories in standardizing procedures for evaluating antibody responses to experimental vaccines, and collecting samples from those evaluations.

Says Esparza, "David's project addresses a critical gap in the field, providing comparative evaluation of immune responses elicited by different candidate vaccines. This allows for a more systematic selection of the most promising products to move forward to clinical evaluation."

PORTRAIT OF A POTENTIAL VACCINE

Montefiori is also addressing a major problem with vaccine testing—the lack of standard reference HIV strains against which researchers could test how well their experimental vaccines stimulate antibody production against the virus.

"Scientists tend to test their serum samples against a small number of HIV strains that are sensitive to neutralization," he says. "That's fine if you want to know basically whether the vaccine neutralizes virus. But the results are muddy because of the difference between those artificial viruses and the real-world viruses that the antibodies really need to neutralize."

By developing refined tests and clinical trial designs, Montefiori's research team aims to give vaccine developers a more specific measure of vaccine effectiveness. "Before, we'd only know if a vaccine was hitting a home run; we wouldn't know if it had only reached first base," says Montefiori. Just slamming a solid single with a vaccine would still be important, he emphasizes.

"We don't expect to have neutralizing antibodies potent enough to block infection altogether," he says. "But even a good partial immune response might reduce viral replication, lowering blood levels and enabling the person to remain healthier. And because they don't have much virus in their blood they would be less likely to transmit, indirectly blocking the chain of transmission."

Also looking to the future, Weinhold believes that the long-desired AIDS vaccine may wind up being a multiple. "I see a cocktail vaccine approach as being more feasible," he says. "The type of vaccine that triggers the appropriate T-cell response may not be good at eliciting antibodies. Thus, although the ideal vaccine is a single shot, the best approach may turn out to be a heterologous 'prime-boost' method incorporating multiple vaccines."

Despite such prognostications, CHAVI researchers admit that the final form of a vaccine, or even its basic feasibility, remains only a cloudy promise. Even Haynes, who is himself working on new envelope-based vaccines with Harvard's Joseph Sodroski, cautions that "We have never guaranteed, nor can the field guarantee, that a vaccine can be made. But we will answer those questions, so that either the money can be invested in making vaccines because we have found enabling technology—or the money can be put into other preventive measures if a vaccine can't be made."

Either way, he vows, CHAVI will throw all its might into the quest for answers, to help the world clearly see the best possible path to curtail the AIDS pandemic. And so the hunt goes on. □


"WHAT IS NOT CURED BY THE KNIFE MAY BE CURED BY FIRE." —HIPPOCRATES

HOT STUFF

An ancient approach to tumor treatment is making waves in 21st-century cancer care

BY JUNE SPENCE

Physicians have long sought to harness the therapeutic value of heat to treat cancer. There are records of ancient Egyptians using a device called a fire drill to cauterize breast cancers, though they deemed them incurable. In the mid-1800s an American surgeon, noting tumor shrinkage in some patients with high fever, began deliberately infecting his cancer patients with bacterial extracts to induce a temperature spike, with mixed results.

In the 1970s, successful experimentation by radiation biologists spurred widespread interest in hyperthermia, recalls Mark Dewhirst, DVM, PhD, professor of radiation oncology and director of the hyperthermia program at Duke. "Everybody was pursuing it then. But it was like a frontier town in that there were no controls to speak of and no training. Temperatures weren't measured; they just turned the power up until the patient said ouch! Or if they did measure temperature it was in one selected point within the tumor, fairly meaningless information."

HYPERTHERMIA'S EFFECTIVENESS HAS BEEN ESTABLISHED. THE CHALLENGE LIES IN "PRESCRIBING" A THERAPY WHOSE EFFECTS ARE SO VARIABLE.

Indeed, despite reports of success, the technical challenges of controlling the power of heat have kept hyperthermia largely out of mainstream cancer treatment—even today, it's usually available only through clinical trials. But the therapy has come a long way, thanks in no small part to over two decades of Duke's leadership in the study and application of heat to boost the effects of radiation and chemotherapy. Launched in 1984, Duke's program has received continuous funding from the National Cancer Institute (NCI) since 1987 and is now the largest of its kind in the world.

Today, earlier scattershot methods of hyperthermia delivery have given way to precision technologies developed or refined at Duke, including a magnetic resonance imaging (MRI) device tweaked to create a 3-D temperature map of the tumor and its environs; microwave antennae that beam heat to precise points in the body; and a tiny fat bubble, or liposome, designed to leak its chemotherapy drug cargo as it reaches the desired temperature and location within the tumor. Such technologies enable better targeting and destruction of tumors—up to 10 times better than with standard therapies. Duke research also is yielding important data such as clear-cut dosing and temperature guidelines for hyperthermia. Together, these advances are moving hyperthermia into the established repertoire of cancer therapies for the first time in the history of modern medicine.

TURNING UP THE HEAT

Hyperthermia works in several ways. Heat opens pores in the tumor's already leaky blood vessels, enabling chemotherapy to more effectively penetrate. Heat also boosts the level of oxygen inside a cell—aiding the proper functioning of radiation and chemotherapy—and decreases the level of DNA damage repair that chemotherapy and radiation induce in cancerous cells. Studies demonstrate a significant reduction in tumor size when hyperthermia is combined with radiation or chemotherapy, results far greater than when the therapies are employed without the use of heat.

While the effectiveness of hyperthermia has been established, the challenge lies in "prescribing" a therapy whose effects are so variable, says Dewhirst. Physicians need guidelines for optimum temperatures and heating times for specific cancers, and they need access to technologies that allow not only consistent delivery but accurate temperature gauging.

"With radiation you can calculate where the dose goes because we know how radiation is absorbed in tissue," Dewhirst explains. "But when it comes to hyperthermia, you're using microwaves, ultrasound, or radiofrequency heating to deliver energy into the body, and there the characteristics of the tissue make a big difference." Lungs are difficult to heat, for example, because the airy tissue doesn't conduct microwaves or ultrasound well.

"The orientation of organs and the shape and size of the body also influence how energy is deposited into the tissue," Dewhirst continues. "And just because you deposit the energy there doesn't mean that it's going to heat the tissue, because the body responds by increasing its blood flow, trying to carry the heat away."

Kimberly Blackwell, MD, a Duke oncologist who has seen dramatic results in clinical trials using hyperthermia to treat recurrent and locally advanced breast cancers, likens the process to "putting a frozen dinner in a microwave, where what can happen is the middle stays frozen while the edges are fried to a crisp. Imagine trying to get absolutely even heat in that situation with blood flow going in all directions. It's pretty hard to do!"

Moreover, the response of the body to thermal stress varies from patient to patient. "The bottom line is you cannot calculate the temperatures in hyperthermia based on some standardized formula," says Dewhirst. "You have to measure them in real time."

MINIMAL INVASION

Until recently, the only practical way to do that was to insert a probe into the tumor or nearby tissue and keep it there throughout the treatment. "We'd like to get away from that and go toward noninvasive thermometry," says Dewhirst. "[Invasive methods] take a lot of physician time, and of course, patients don't like being stuck."

Noninvasive scanning not only spares the patient the discomfort of a probe, but provides a more comprehensive picture of the area, he adds. "If we have three-dimensional information that shows us what the temperatures are throughout the tumor, we can better control the heating as well as make it easier for technologists to perform the treatment."

Two of the hyperthermia program's current projects are zeroing in on just that. In one, a team of biomedical engineers, physicists, and radiation oncologists at Duke have created a noninvasive "imaging thermometer," an adaptation of the traditional MRI. It measures a tumor's temperature in part by detecting how fast water moves inside the tissue (water moves faster as it heats up). The resulting on-screen image is a three-dimensional temperature map, with the hottest regions appearing in red and the coldest in blue.

"THE MRI WE'VE ADAPTED IS A TYPICAL MODEL," SAYS MARK DEWHIRST. "WE ENVISION A PLUG-IN THAT SOMEONE COULD BUY AND ADD ON TO AN EXISTING MACHINE." SINCE MANY FACILITIES ALREADY HAVE MRI UNITS, THIS COULD HELP MAKE HYPERTHERMIA MORE BROADLY AVAILABLE.

By interfacing that data with the heating device, researchers aim to provide real-time information that makes it easier to see and control the heating of the tumor. Once optimum temperatures are achieved, the tumor is treated with radiation or chemotherapy.

In a related project, Duke's multidisciplinary team is seeking to develop the imaging thermometer so it can one day be offered as an attachment. "The MRI we've adapted is a typical model," says Dewhirst. "We envision a plug-in that someone could buy and add on to an existing machine." Since many facilities already have MRI units, this could help make hyperthermia more broadly available.

"SARCOMA IN A DOG IS INDISTINGUISHABLE FROM SARCOMA IN A HUMAN. THEY BEHAVE THE SAME WAY IN THE BODY." —MARK DEWHIRST, DVM, PHD

HOT DOGS

Humans aren't the only creatures benefiting from advances in hyperthermia. In a two-decades-long partnership that has profited both people and pets, Duke hyperthermia researchers have worked with the North Carolina State University veterinary school in Raleigh, North Carolina, to study hyperthermia in dogs—while offering the advanced treatment to animals suffering from malignant tumors.

Currently, Duke and NC State researchers are collaborating on a sarcoma trial, examining how hyperthermia affects blood flow and oxygenation of tumors in pet dogs. "We get a tremendous amount of information from these pets," notes hyperthermia program director Mark Dewhirst, who trained in veterinary medicine as a route to biomedical research. "Sarcoma in a dog is indistinguishable from sarcoma in a human. They behave the same way in the body."

GOING TO EXTREMES

Another device recently devised at Duke to help better target and heat tumors is a hyperthermia "cuff" that encircles limbs with tumors. The cuff contains multiple antennae that can be adjusted to precisely aim microwaves at the enclosed tumor, ensuring a precise dose of heat reaches its intended target. Two clinical trials are testing the use of the cuff in combination with radiation or chemotherapy for patients with sarcomas, tumors of connective tissue that have a propensity to recur locally and require potentially disfiguring resections when located on the arms or legs.

Hyperthermia has also found a role in treating melanoma of the extremity, another type of tumor that tends to recur in a local or regional pattern. Doug Tyler, MD, a Duke surgical oncologist, explains, "With most extremity melanomas, surgical excision is curative. However, approximately 5 to 10 percent of the time, the melanoma will recur in multiple spots but still be confined to the extremity without any evidence of spread elsewhere in the body. To effectively remove the cancerous tissue, you may have to do something really disfiguring such as perform an amputation, or deliver a high dose of regional chemotherapy to the extremity where the tumor is located."

It's in this latter situation that hyperthermia has found its biggest role, Tyler notes. "Regionally applying heat at the same time that you are giving the regional chemotherapy not only markedly improves the tumor responses, but also increases the durability of the tumor remission. The results are generally good enough that amputation is rarely needed."

In 1995, Tyler was asked to set up a regional therapy program in melanoma at Duke. Although the regional infusion treatments they gave involved the use of hyperthermia, the program developed independently of Dewhirst's efforts until 2001. "By then we'd become very interested in the different patterns of response," Tyler recalls. "In about half the patients we could get complete responses for long periods of time, 40 percent were partial responders, and about 10 percent didn't respond at all. To improve on these results we needed to take things back to the laboratory and explore ways to optimize this form of treatment at a basic science level."

To better understand the role of hyperthermia in regional infusion, Tyler and colleagues developed a regional chemotherapy animal model of recurrent extremity melanoma in rats. They also began attending the annual hyperthermia retreat that Dewhirst had set up to encourage the cross-pollination of ideas. "We presented some of our early animal data there, which quickly led to several preclinical collaborative studies with Dr. Dewhirst's group. The results of these studies served as the basis of a phase I/II clinical trial that combined regional chemotherapy treatment using melphalan with hyperthermia to 38.5 degrees centigrade. This trial was included as part of Dr. Dewhirst's recently refunded hyperthermia program project grant with the NCI." The collaboration has continued to grow, as Tyler currently has two active regional chemotherapy and hyperthermia trials for advanced extremity melanoma and four more in various phases of the development or approval process.

BREAST CANCER A HOT TOPIC

Results of a Duke study published in 2005 and led by Ellen Jones, MD, PhD, radiation oncologist and a clinical director of Duke's hyperthermia program, could change the standard of care nationally for patients with chest wall tumors. In the study, hyperthermia given before radiation shrank tumors completely in 66 percent of the patients, most of whom had post-mastectomy chest wall recurrences of breast cancer. By contrast, radiation therapy alone destroyed tumors in just 42 percent of patients. Duke is currently using hyperthermia with radiation as standard therapy for recurrent chest wall cancers, and it has been approved for Medicare and Medicaid patients.

"Adding hyperthermia to standard radiation gives us a strategy to get more mileage out of a modest dose of radiation for previously treated patients, who cannot tolerate a full dose," says Jones.

Reducing toxicity is also desirable in chemotherapy, where the powerful drugs that kill cancer cells could also damage the heart and other tissues. Hyperthermia is useful here as well. Though it's not yet fully understood why, heat increases the rate of a drug's uptake into a cancer cell. It also increases the DNA damage chemotherapy inflicts on the cell by interfering with enzymes that repair such damage.

"IN THE LAST YEAR WE'VE HAD MORE INTEREST IN HYPERTHERMIA THAN EVER.... THE PUBLIC IS ASKING FOR IT. PEOPLE SEE THE PROMISE IN IT."

In the 1990s, Dewhirst began collaborating with Duke materials scientist David Needham, PhD, on the use of heat-sensitive liposomes containing chemotherapy drug in combination with hyperthermia. Liposomes had not lived up to their early promise of targeted drug delivery because researchers had not succeeded in getting them to dump their contents at the tumor site. Likewise, hyperthermia was not yet showing significant efficacy with chemotherapy; the high temperatures needed to maximize the combination weren't achievable.

Dewhirst and Needham learned that hyperthermia greatly improved drug delivery via the liposome. Heating the tumor area drew liposomes out of the bloodstream and to the tumor. Moreover, an achievable level of heat greatly enhanced leakage of drug out of the liposome and into the tumor.

Women with locally advanced breast cancer, which is often resistant to traditional treatments, were the first beneficiaries of this combined therapy. In a Duke clinical trial whose results were first presented in 2002, the combination therapy halted tumor growth in all of the women and shrunk tumors in half the women. A third of the women showed a complete clinical response, meaning their tumors were reduced to undetectable levels.

"By delivering the drugs to the precise site of the tumor, and releasing them at a precise point in time, we're able to direct their tumor-fighting abilities where they're needed most," explains Jones. "It really is, in the purest sense, targeted therapy," adds Blackwell.

Thirty times more of the chemotherapy drug doxorubicin can be safely delivered via the heat-sensitive liposome than through the conventional intravenous method, where the risk of toxicity requires a smaller dose. Needham has developed a new version of the liposome that melts even faster than the previous one, dumping its contents into the tumor within 20 seconds at 41 degrees Celsius (104 degrees Fahrenheit). In a current phase I clinical trial, women with chest wall recurrences of breast cancer are receiving doxorubicin via this more thermally sensitive liposome.

Controlled delivery is made possible through a unique treatment table designed and built by Duke engineer Thaddeus Samulski, PhD, to isolate and heat the cancerous breast tissue, which is immersed in a pool of salt water. Radio frequency energy controlled by software raises the water's temperature and distributes heat into the breast. The heat-seeking liposome is thereby drawn to the site of the tumor, where at a precisely determined point the heat melts the casing, releasing the drug.

A patient once dubbed the device "the booby Jacuzzi," and the name has persisted, but Blackwell thinks it doesn't do justice to the work involved. "This is a very complex way of heating the breast. The fact that we can now increase drug delivery by accurately and thoroughly heating a tumor that sits in the breast took some 30 to 40 years of work and multiple areas of expertise."

A WARMING TREND?

Hyperthermia research at Duke is expected to continue apace, with plenty of projects in the works or on the drawing board. Further developing noninvasive thermometry and viewing drug delivery in real time are among the goals the program is pursuing. Duke's current clinical explorations include an international phase III trial adding hyperthermia to the current standard of care for locally advanced cervical cancer to see if it reduces mortality.

"The trial compares the best conventional therapy, which is platinum and radiation, plus or minus heat," says Dewhirst. "It's a really important trial for us." While screening programs have lowered the rate of locally advanced cervical cancer in the U.S. and many Western countries, worldwide it is the number-one cancer killer of women. And even in the U.S., the cure rate is low for women whose cervical cancer

isn't diagnosed in its early stages.

Other projects in development include a formulation of the liposome that contains cisplatinum. Cisplatinum is often used in combination with radiation therapy for colorectal and esophageal cancers as well as cervical cancer. "Another disease where platinum might be useful is ovarian cancer," says Dewhirst. "We've done a couple of phase I trials where we put platinum-containing saline solution into the peritoneal cavity through a catheter in the abdomen and then heated the fluid. These trials had pretty impressive anti-tumor effects, but the treatment is technically difficult, and leaving the catheter in place over several weeks of treatment can cause complications such as infections. The liposome might help reduce these problems because we'd give it systemically but only heat the precise area of the body."

Despite hyperthermia's demonstrated efficacy, Duke's investment in the therapy far outflanks that of other medical programs. "There's a lot of tech and industry mindset feeding the belief that you'll make a bigger impact developing new and novel drugs than in making existing drugs work better," Tyler ventures. "That may be why you haven't seen a lot of other places sustaining a hyperthermia program."

"THE FACT THAT WE CAN NOW INCREASE DRUG DELIVERY BY ACCURATELY AND THOROUGHLY HEATING A TUMOR THAT SITS IN THE BREAST TOOK SOME 30 TO 40 YEARS OF WORK AND MULTIPLE AREAS OF EXPERTISE." —KIMBERLY BLACKWELL, MD

Dewhirst observes, "Avastin doesn't have eight positive phase III trials. Gleevec doesn't. So what is it about hyperthermia that creates this apathy? One big impediment is the technical difficulty of doing it.

"We try to take the long-term view; there's a great deal of promise here, but there's a lot to be worked out to make it happen. We decided to stick with it and work out the problems. Along the way, we picked up the liposome, which has opened the door to new diseases and approaches we've never done before."

That could explain why, after over 20 years of quietly flourishing, the program is garnering so much recent attention. "In the last year we've had more interest in hyperthermia than we've ever had," Dewhirst says. "I've done lots of interviews this year. After an interview with CBS News aired [in April], I had hundreds of phone calls and e-mails. The public is asking for it. People see the promise in it." □

For more information on hyperthermia treatment and clinical trials at Duke, visit hyperthermia.mc.duke.edu.

Reaching out from the ivory tower

Scientists and other academics can make a big difference in the world—and not just through their studies.

by Peter Agre, MD

As I write this, I have just returned from the fall meeting of the Committee on Human Rights of the National Academies, a committee which I currently chair. Although it has been in existence for some three decades, few people know about the committee's important work, which is usually done behind the scenes. Our members and correspondents, including Nobel laureates and other leading scientists, write letters and contact colleagues and others to advocate for particular scientists, engineers, or health care workers who are unjustly imprisoned or threatened with imprisonment. (We've found this quiet approach to be more effective than aggressive means that would force target governments to become defensive.)

Although time-consuming and often heart-wrenching, my role as chair is very important to me—even though I wouldn't have anticipated leading such an effort earlier in my career. While long a private supporter of human rights, I was, like many other academics, absorbed primarily in the day-to-day challenges of my work. And so it was a personal matter that called me to public advocacy—the arrest and later the imprisonment of a former colleague, Thomas Butler, MD, on what I and many others considered unjust charges stemming from the disappearance of plague samples from his lab. Since then, I have been active in advocating for numerous others whose plights have been taken up by the committee, including many who have been imprisoned or threatened because they have applied their skills to help victims of torture and other populations whose basic human rights have also been violated.

The Butler case first brought me to the committee; what has kept me involved is the conviction of just how important such activism is—that taking action is, quite simply, the right thing to do. I think most of us would agree that upholding political, civil, and other human rights is important. But it is only when we actively defend those principles that we can help secure their benefits for all people.

FROM INFORMATION TO IMPACT

As an academic medical center, Duke Medicine supports the same human rights that the committee seeks to uphold—those of freedom of expression and free scientific exchange. Our faculty, trainees, and students widely publish their research on fundamental biology, the biology of health and disease, new diagnostic tools and treatments, and the practice and delivery of health care itself, and our faculty share their findings in lectures across the country and around the globe.

But sometimes lecturing and publishing aren't enough. The rights of freedom of expression and freedom of scientific exchange are accompanied by the right of all people to benefit from scientific advances. Therefore, our responsibility is not merely to generate and exchange new knowledge, but to apply that knowledge to make a difference in the world. If we give little attention to what is happening beyond our immediate sphere, we leave our work's true potential unfulfilled.

That is why I am especially pleased by the leadership Duke has shown in creating the Duke Global Health Institute (GHI), launched this spring and now led by Michael Merson, MD. Created to address health disparities at home and worldwide, the GHI is expressly committed not only to study such issues, but to engage in a wide range of service projects designed to tackle health disparities head-on, both by sharing our expertise and by learning from our colleagues and the local populations.

At its core, the GHI is upholding one of the most fundamental human rights—the right, as the Universal Declaration of Human Rights (adopted by the United Nations in 1948) puts it, "freely . . . to share in scientific advancement and its benefits." Unfortunately, many people in the U.S. and around the world do not enjoy the improvements in medicine and health that scientific advances can bring. Instead, inequalities abound. The "Green Revolution" that dramatically increased food production may be

If we give little attention to what is happening beyond our immediate sphere, we leave our work's true potential unfulfilled. That is why I am especially pleased by the leadership Duke has shown in creating the Duke Global Health Institute.

allowing food donations to countries and peoples battered by environmental devastation and political upheaval, but it has not allowed them to reclaim their once productive lands. The "Genomic Revolution" may be allowing physicians to choose appropriate, specific treatments for certain patients with cancer or HIV, but there are millions in Africa and Asia who lack even the most rudimentary of treatments for HIV and AIDS. In our own country, and even right here in Durham, there are health disparities caused by lack of insurance, lack of access to care, and even simply race itself, since studies have shown that patients of different races are offered different treatments despite presenting with identical symptoms.

Such health disparities stem from more than just problems with health care delivery. As the team responsible for drawing up recommendations for a Global Health Initiative at Duke pointed out in their report to Provost Peter Lange and Chancellor for Health Affairs Victor J. Dzau, "[Disparities] are the result of political instability, poverty, and social factors in addition to the lack of quality health care. But … poor health is also a cause of poverty, political instability and contagion." For that reason, any efforts to address health disparities must also address the broader conditions that contribute to them.

Toward that end, the GHI has been established as a university-wide initiative—involving not just the medical and nursing schools, but leading researchers working in policy, law, business, divinity, the environment, and other areas of the university that examine the range of local and global issues that also affect health. This multidisciplinary effort will deliver greater understanding of the complexities of global health inequalities. At the same time, Duke researchers, clinicians, trainees, and students will be working on the ground both here at home and around the world to advocate for needed change, to learn and to apply what we learn to directly improve the health of the underserved.

INSPIRING EFFORTS

The Duke Global Health Institute is an ambitious, global approach to addressing a global need and reflects our responsibility not only to examine, but to improve the world in which we live. Given the institution's significant commitment to these efforts, I believe that Duke will set an example for other institutions. I also hope that Duke's efforts will inspire individuals to do what they can to reduce disparities and reverse injustices.

As an academic institution we are not equipped to save the world. But as an academic institution we can and should work toward that idealistic goal. As physicians and scientists, we know our advances have the potential to help improve lives. It is our responsibility to share the information we gain, to learn from others, and, when possible, to apply what we have learned for the benefit of all.

And sometimes we need to step outside of our academic work. During the recent meeting of the Committee on Human Rights, we were visited by an academic whose freedom the committee helped secure. But even more powerful than his message of thanks was that of my taxi driver later that day. The driver happened to be from the same poor African country as our guest, and I asked if he knew who the man was. The driver became very animated, and said, "Oh yes, he is a national hero." I explained how the committee had helped, and the driver said, "Thank God for your work. You must not stop, you must help the others."

That is a good message for all of us, I think.

Peter Agre, MD, who shared the 2003 Nobel Prize in Chemistry for revealing the molecular basis for the movement of water into and out of cells, is vice chancellor for science and technology at Duke. A member of the National Academy of Sciences since 2000, he has chaired the National Academies' Committee on Human Rights since 2005.

The opinions expressed in "Perspectives in Medicine" are those of the author and do not necessarily reflect those of Duke University Medical Center as a whole.

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.**

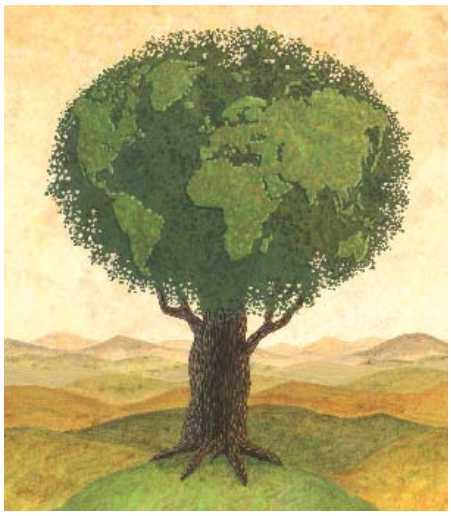
Hubert Trust funds education and research in global health

"The Hubert family's partnerships in global health have been characterized by a wonderful spirit of collaboration and service, knowledge of the complex issues involved, respect for other cultures, and a genuine desire to raise awareness, understanding, and interest in global health among future leaders." —Duke University President Richard H. Brodhead

A $5-MILLION GIFT to Duke's Hubert-Yeargan Center for Global Health will expand research, service, and educational opportunities in global health for students and health care professionals at Duke and neighboring colleges and universities.

The gift, from the Hubert Trust of Atlanta, Ga., is intended to foster collaborations with other organizations and institutions to make the best use of resources, expertise, and experience. The program previously received major gifts from the Hubert Trust, Yeargan Charitable Foundation Trust of Garner, N.C., and Gary Hock, owner of G.M. Hock Construction Company.

Under the direction of G. Ralph Corey, MD, the Gary M. Hock Distinguished University Professor of Global Health, the Hubert-Yeargan Center partners with clinical and research sites in Tanzania, Kenya, Sri Lanka, Brazil, Thailand, and many other developing countries.



"The Hubert family's partnerships in global health—with Duke and many other academic and charitable organizations—have been characterized by a wonderful spirit of collaboration and service, knowledge of the complex issues involved, respect for other cultures, and a genuine desire to raise awareness, understanding, and interest in global health among future leaders," says Duke University President Richard H. Brodhead. "We are very grateful for their vision and generosity to Duke."

Richard N. Hubert, trustee, said the Hubert Trust was encouraged by Brodhead's commitment to global health and by the launch this past summer of the Duke Global Health Institute.

"We found what we had started at Duke with Dr. Corey to be a worthy program, and with President Brodhead's interest we saw a real opportunity for Duke to become a principal player in global health," says Hubert, who is a 1957 graduate of Trinity College.

Corey's program had its beginnings in 1986 when Duke Medicine's Division of Infectious Diseases began several international projects in order to study HIV/AIDS, malaria, tuberculosis, and other diseases and provide international health education and service opportunities for its residents and fellows.

The center's mission is to improve the health of people throughout the world by providing experiential learning opportunities in developing countries for students and health care professionals and by supporting collaborative research to reduce the burden of disease.

Other global health programs endowed by the Hubert Trust include the Rollins School of Public Health at Emory University and agricultural partnerships with charitable and faith-based organizations in North Korea and Haiti.

V Foundation funds Duke-UNC cancer collaboration

Collaborative research between the Duke Comprehensive Cancer Center and the University of North Carolina's Lineberger Cancer Center is the goal of a **$2-million grant** from the V Foundation. Duke's Joseph Nevins, MD, and UNC's Charles Perou, MD, will work together on "Programs to Develop Genomic Strategies for Personalized Cancer Treatment." Other Duke recipients of V Foundation grants for 2006 are Anil Potti, MD, an assistant professor of medicine and member of the Duke Institute for Genome Sciences & Policy, who received $600,000 for his work on targeted therapies in non-small cell lung cancer, and Robert Greiner, MD, who received $225,000 as part of a Jim Valvano Fellowship in Pediatric Cancer Research.

Brumley family endows neonatal research at Duke

Duke's McGovern-Davison Children's Hospital and Health Center received the second largest gift in its history this fall from the Atlanta-based Zeist Foundation. The **$5-million** gift will fund research and two endowed professorships in neurodevelopmental biology at the Duke Neonatal Perinatal Research Institute (NPRI). The Zeist Foundation was established by the family of the late George W. Brumley Jr., MD, Duke's first director of neonatology, who with current director Ronald N. Goldberg, MD, co-founded the Duke NPRI. The two professorships and the Duke NPRI will be named to honor Dr. Brumley and his late wife, Jean Brumley.

A father honors his son—with a gift for the future

Robert T. King Jr. of Hickory, North Carolina, says he sought to match the dedication and integrity of his son Robert T. King III when he decided to establish a fund that will provide scholarships for Duke MD/PhD students. The younger King is a 1984 graduate of Duke's Trinity College who received his Duke MD in 1988. He is now a retina specialist with the Georgia Eye Institute in Savannah.

"Duke's emphasis on research provided an excellent environment for learning how to think critically," says King. "Critical thinking, combined with a commitment to the patient, will result in better care. I'm grateful for the education my son received, and I hope we can extend those same chances to other dedicated students."

Initially, King had planned to make a gift through his estate, but then learned he could donate a townhome the family owns in Hilton Head, South Carolina. Proceeds of the sale will be combined with matching funds available through the Duke University Financial Aid Initiative to establish the **$1-million** King Family scholarship endowment.

King, who also has three daughters and 11 grandchildren, says he views his gift as an investment in research and patient care that may help others.

"I'm a businessman, and I look at this not only as a gift, but as an investment—a way to light a fire in research against cancer and other diseases," says King. "I hope it will one day help my family and other people too."

Duke currently has one of the nation's leading programs for MD/PhD students, who typically spend seven years earning the dual degree and go on to careers as biomedical researchers. Duke is known for producing scientists who are grounded in clinical medicine and able to translate basic research into new therapies for prevention and treatment.

As of October 2006, Duke Medicine has received $8 million in gifts toward its goal of raising $12 million for the Financial Aid Initiative by 2008. More information about the Financial Aid Initiative is available online at medschool.duke.edu/fai.

Honoring the Semans legacy

Mary Duke Biddle Trent Semans became an honorary member of Duke's Department of Surgery in September when she received a white coat—the traditional symbol of medicine. The gift was presented by Chancellor Victor J. Dzau, MD, above right, and Chair of Surgery Danny Jacobs, MD, left, at a dinner held to remember the late James H. Semans, MD, who with Mrs. Semans was a longtime supporter of the Division of Urology. Dr. Semans was a Duke surgeon and urologist known for his ahead-of-its-time interdisciplinary approach to patient care. A financial commitment from the Division of Urology, combined with gifts from Dr. and Mrs. Semans, have established the James H. Semans, MD Endowed Professorship in Urology, the first such distinguished position in urology at Duke.

No boundaries to expertise

Michael H. Merson, MD, an internationally recognized expert in the study of HIV/AIDS, has been named director of the newly created Global Health Institute at Duke University.

The new institute will promote interdisciplinary education, research, and care delivery to address health gaps between the poor and the affluent by incorporating every field on campus: environment, medicine, law, nursing, engineering, business, natural and social sciences, and divinity.

"The Global Health Institute exemplifies the kind of cross-field collaboration that's rare elsewhere but relatively common here," says Richard H. Brodhead, PhD, president of Duke University. "I am extremely pleased that Dr. Merson will lead this visionary new program to address health disparities in Durham and around the world."

Victor J. Dzau, MD, chancellor for health affairs and president and CEO of the Duke University Health System, adds, "We must address issues of global health in under-resourced communities and nations. We see this not only as a moral imperative but also as a key to global stability."

Merson was selected after an extensive international search, says Provost Peter Lange, the university's chief academic officer. "I am delighted to have the search committee recruit someone of Dr. Merson's stature to lead the Global Health Institute," Lange says. "As a nationally recognized global health expert who has spent his career at some of the world's top health organizations, Dr. Merson brings a wealth of experience and knowledge to Duke."

Merson most recently served as the Anna M.R. Lauder Professor of Public Health at Yale and director of Yale's Center for Interdisciplinary Research on AIDS. Previously he spent nearly 20 years at the World Health Organization (WHO), including five years as director of the WHO's Global Program on AIDS. A widely published researcher and member of the Institute of Medicine of the National Academies, he has served on various NIH review panels and advisory committees, is a consultant to the World Bank for its HIV/AIDS projects in various countries, and has received the Surgeon General's Exemplary Service Medal and the Arthur S. Flemming Award for distinguished government service.

Read an interview with Merson on page 64.

Developing Duke Medicine

Michael J. Morsberger, who has led large-scale, successful fundraising efforts at Johns Hopkins Medicine and the University of Virginia, has been named vice president for Duke Medicine Development & Alumni Affairs.

Morsberger most recently served as associate vice president of development and executive director at the University of Virginia (UVa) Health System and UVa Health Foundation in Charlottesville. At UVa, he was instrumental in planning the health system's $500-million campaign and served as a senior member of the university's development team in the midst of a $3-billion campaign, currently the largest announced fundraising campaign goal at a public university in the United States.

"I am delighted that Mike is joining Duke Medicine," says Chancellor Victor J. Dzau, MD. "Philanthropy is a major source of funding here, and we have an ambitious vision for the future. We believe Mike will be instrumental in forming the development strategy and implementing the plan to bring that vision to fruition."

"Every member of the search committee was captivated by his manner and inspired by his conviction and intensity," adds medical school dean R. Sanders Williams, MD. "He will bring not only tremendous experience, but some exceptional abilities to this vital role."

Morsberger says he is looking forward to building philanthropic partnerships between benefactors and faculty in order to fuel novel medical research, support patient care, and educate the next generation of nurses and doctors.

"Duke Medicine has a long history of attracting both the resources and the wisdom of major donors," he says. "The next great campaign for Duke will require the thoughtful stewardship and involvement of past investors as well as an invitation to never-before-engaged alumni, parents, and others to join us in changing the face of modern medicine."

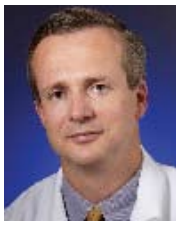
Research powerhouses

Robert M. Califf, MD, who directed the Duke Clinical Research Institute (DCRI) for the past 10 years, has been named director of the new Duke Translational Medicine Institute (DTMI).

A world-renowned leader in the fields of health outcomes, quality of care, and medical economics, Califf led DCRI efforts for many of the best-known clinical trials in cardiovascular disease. He also serves as Duke's vice chancellor for clinical research and professor of medicine in the Division of Cardiovascular Medicine.

Robert Harrington, MD, a professor of medicine in cardiovascular medicine at Duke, will succeed Califf as the new director of the DCRI. A distinguished physician-scientist, Harrington has been serving as the co-director of cardiovascular research and the leader of cardiovascular clinical trials at DCRI, the world's largest academic clinical research organization.

"Bob has played an instrumental role in making the Duke Clinical Research Institute what it is today, and he is, without any doubt, the single most qualified individual to lead it in the next phase of its evolution," Califf says. "He is well known, both nationally and internationally, as an inclusive leader who seeks collaboration as the primary method to advance the field."



"I am honored to be chosen to lead the Duke Clinical Research Institute at this challenging yet exciting time for academic medicine and biomedical research," Harrington says. "DCRI has a well deserved reputation for excellence and innovation in clinical research that we intend to both continue and expand."

For more information on the DTMI, see page 4.

Vice-dean for education transition

Edward G. Buckley, MD, was named interim vice-dean for education at the Duke University School of Medicine in October.

Buckley, a member of Duke's faculty since 1983, is currently a professor of ophthalmology and pediatrics and division chief of pediatric neuro-ophthalmology. He has been involved in developing and maintaining the medical school curriculum as chair of the curriculum committee, associate dean for undergraduate medical education, and as a member of the admissions committee.

In his new role Buckley will be responsible for the educational quality of the medical doctor (MD) program, the physician assistant program, and the physical therapist training program. He will also oversee the admissions department, the curriculum office, student affairs, the medical center library, and anatomical gifts.

"Dr. Buckley has an outstanding record of clinical, administrative, and research achievements at Duke, and is well-suited to serve in this role," said R. Sanders Williams, dean of the School of Medicine, in announcing the appointment. "He knows the institution and the medical school very well, and has shown imagination and creativity in several challenging roles, perhaps most notably in leading our curricular reforms."

Buckley succeeds **Edward Halperin, MD**, who became dean of the University of Louisville's School of Medicine November 1. Halperin was formerly professor of radiation oncology, pediatrics, and medical education, and associate vice chancellor for academic affairs at Duke, and had also served as department chair of radiation oncology. Appointed vice dean in 2002, he was instrumental in shaping and overseeing the educational programs of the medical school, in particular strengthening its dual degree programs and implementing fresh ideas into the medical student curriculum.

"His service to Duke also includes innumerable, and often unheralded, acts of sound judgment in his leadership roles," says Williams. "He has been a valued friend and key advisor to me in the most important and difficult decisions I have faced as dean."

Halperin also served as an unofficial historian of Duke Medicine, including spearheading a project that led to the creation of "Heritage Hall," a hallway in the administration area that displays images of historical leaders of Duke University Medical Center.

Directing genetics

Marcy C. Speer, PhD, has been named interim director of the Duke Center for Human Genetics. She will oversee the efforts of center researchers to understand genetic influences on human health.

Speer is a professor of medical genetics in the Department of Medicine and also holds appointments in Molecular Genetics and Microbiology and in Biostatistics and Bioinformatics. Her research has focused on uncovering genetic and environmental contributions to neurodevelopmental conditions, including spina bifida, anencephaly, and Chiari malformations, and she also has conducted extensive studies of muscular dystrophy.

Speer was a consensus choice, says Dean R. Sanders Williams, MD. "She has the international scientific stature, leadership traits, and communication skills we expect of leaders at Duke, and she has earned the trust and respect of faculty colleagues within the Center for Human Genetics and more broadly within our Institute for Genome Sciences & Policy and departments."

Headlining the news

Doug Stokke has been named assistant vice president for communications at Duke Medicine, where he will oversee the organization's news and internal communications functions.

Stokke most recently served as vice president, CNS/Neurology Pharmaceutical Communications, at Johnson and Johnson Pharmaceutical Services. He joined the company in 2004 as vice president, media relations and management communications.

"Doug brings 25 years of communications experience spanning many areas of health care, from hospitals to academic medicine to the pharmaceutical industry," says Gwynn T. Swinson, JD, vice president for communications and government and community relations. "His deep knowledge of health care and his record as a senior counselor and strategist for several complex organizations make him an excellent choice to lead Duke Medicine's communications efforts."

Compliance chief

Tina R. Tyson, JD, former associate general counsel for university compliance at Washington University in St. Louis, was named chief compliance officer for Duke's School of Medicine.

She will develop programs and processes to ensure that the school complies with external laws and regulations as well as rules set forth by Duke's own code of conduct. She will also collaborate with related offices throughout the university in investigating and resolving compliance issues.

"Tina has skill, judgment, and experience with compliance issues in an academic setting, and we are thrilled that she'll be joining our team," says Dean R. Sanders Williams, MD. Tyson replaces Juliann Tenney, who will become director of the new Duke University Compliance and Ethics Initiative.

Scholarly computing

Asif Ahmad, vice president of diagnostic services and chief information officer for Duke University Health System, will take on an additional role as associate dean for academic computing at the School of Medicine, says Dean R. Sanders Williams.

In this new role, Ahmad will be responsible for developing, implementing, and maintaining computing programs that support the School of Medicine's strategic and operational needs and goals.

"Asif has shown himself to be exceptionally capable in aligning our clinical and academic missions," says Williams. "The creation of this position recognizes the importance of informatics and academic computing in all areas of the medical school, including curriculum, imaging, research administration, and compliance. Asif brings extraordinary skills and energy to our leadership team."

Under Ahmad's leadership DUHS has been honored with many national and international awards for computing excellence, including recognition as one of "America's 100 Most Wired" hospitals and health systems from *Hospitals & Health Networks* magazine.

Duke PA on board

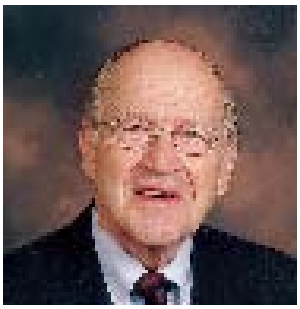
Peggy Riley Robinson, MHS, PA-C, a faculty member in Duke's physician assistant program, was appointed by Gov. Michael Easley to serve a three-year term on the North Carolina Medical Board.

The Medical Board is responsible for licensing, monitoring, and disciplining physicians statewide in order to ensure patient safety. The board comprises 12 appointed members: seven physicians, one doctor of osteopathy, one physician assistant or nurse practitioner, and three members of the public with no medical background.

"I am very pleased that Peggy Robinson has been chosen to serve on the Medical Board," says Lloyd Michener, MD, chair of Duke's Department of Community and Family Medicine. "She is dedicated to providing the best care to her patients, and I know she will apply that commitment to her work as a board member."

Robinson is the first physician assistant to serve on the board who also holds a faculty position. At Duke, she focuses on teaching students about clinical medicine and how to physically assess patients, and she also conducts a primary care practice, treating patients of all ages.

Erich Jarvis, PhD, was selected by *Popular Science* magazine as one of its Brilliant 10 Scientists.



Samuel L. Katz, MD, was honored for outstanding contributions to children's health care.

Tannishtha Reya, PhD, received a Presidential Early Career Award recognizing promising researchers.

Jane S. Richardson was selected as a member of the Institute of Medicine.

Erich Jarvis, PhD, associate professor of neurobiology, has been named to *Popular Science* magazine's Brilliant 10 list of young scientists and researchers to watch. The list appeared in the October 2006 issue.

The scientists listed are extraordinary thinkers who are gaining recognition in their fields, according to the magazine.

Jarvis, who came to Duke in 1998, uses songbirds to study the neurobiology of vocal communication. His research has yielded insights into the genetics and molecular biology of learned vocal communication. Jarvis has also led an international consortium of neuroscientists that proposed a drastic renaming of the structures of the bird brain to correctly portray birds as more comparable to mammals in their cognitive ability.

Samuel L. Katz, MD, Wilburt Cornell Davison Professor and chairman emeritus of Duke's Department of Pediatrics, has received the 2006 Alfred I. duPont Award for Excellence in Children's Health Care.

The award, established in 2001 to honor one person annually who has made a substantial contribution to children's health care nationwide, is presented by Nemours, one of the nation's largest children's health systems.

Katz is one of the original members of the team of researchers who developed the measles vaccine. After his team developed the vaccine, Katz collaborated with government and non-profit organizations to provide it to populations around the globe. Since it was discovered, the vaccine has been credited with saving millions of lives.

Tannishtha Reya, PhD, assistant professor of pharmacology and cancer biology, received a Presidential Early Career Award for Scientists and Engineers at a ceremony July 26 at the White House.

The awards recognize "the most promising researchers in the nation within their fields," according to the White House Office of Science and Technology Policy. In all, 56 researchers received awards.

Reya has significantly advanced the field of stem cell research by demonstrating how "hematopoietic" or blood stem cells maintain their ability to perpetually renew themselves and survive indefinitely. Her discoveries ultimately may enable scientists to grow stem cells in the laboratory and transplant them into patients with blood disorders, immune defects, and select genetic diseases.

Six nurses from Duke University Health System were named to the 2006 list of the "Great 100 Nurses" after being chosen by The Great 100, a statewide peer recognition organization.

The recipients from Duke are: **Mary Ann Fuchs, MSN, RN**, chief nursing and patient care services officer, Duke University Health System and Duke University Hospital; **Debra Hernandez, RN**, chief nursing officer, Durham Regional Hospital; **Nancy Short, DrPh, RN**, assistant dean and assistant professor, Duke University School of Nursing; **Jane Mericle, RN**, clinical operations director, Children's Critical Care, Duke University Hospital; **Kerry Harwood, MSN, RN**, oncology clinical nurse specialist, Duke University Hospital; and **Joanna Smothers**, clinical nurse level III, Telemetry, Duke Raleigh Hospital.

Jane S. Richardson, James B. Duke Professor of Biochemistry, has been elected to the prestigious Institute of Medicine of the National Academy of Sciences for her research into the three-dimensional structures of proteins and RNA.

Richardson is one of a handful of individuals who has excelled in the sciences without holding a PhD; she earned a bachelor's degree in philosophy from Swarthmore College. In 1985, she was awarded a MacArthur Fellowship for her "ribbon" schematic drawings of protein structure. The ribbon drawings have become the basis for widely used computer-generated renderings of protein structure.

Earlier this year, Richardson and colleagues made a significant discovery about small motions inside proteins that lead to much larger changes at the surface, where they affect interactions with other molecules. This adds to a deeper understanding of the basics of protein structure, function and evolution. It could provide a helpful step toward the construction of man-made proteins to treat a wide array of diseases.

Nancy M. Short, DrPh, RN, was appointed as a senior research fellow in the Health Inequalities Program at the Terry Sanford Institute of Public Policy. The program is part of Duke's Center for Health Policy, Law, and Management.

The former assistant dean of the Duke School of Nursing, Short spent 18 months in Washington, D.C. as a Robert Wood Johnson Foundation Health Policy Fellow (RWJF) for Sen. William Frist. Short was the first nurse from Duke to be awarded the RWJF fellowship.

John Weinerth, MD, associate dean for graduate medical education, received a 2007 Courage to Lead Award from the Accreditation Council for Graduate Medical Education (ACGME) for his outstanding leadership of GME programs. The award was given to only three designated institutional officials this year.

James H. Carter Jr., MHS, PA-C (left), with 2006 Duke PA Hall of Fame inductees: **Lovest T. Alexander Jr., MHS, PA-C; James Schmidt, BHS, PA-C; Lisa Shock, MHS, PA-C; Margaret Schmidt, EdD, CLS (honorary Duke PA)**; and **Roger Whittaker**'s daughter, Holly, who received the honor in his stead.

Former nursing school dean **Ruby Wilson, EdD, RN**, was selected to receive the prestigious University Medal for Distinguished Meritorious Service.

Darell Bigner, MD, PhD, was honored by Lund University in Sweden.

Weinerth, who oversees Duke's 71 ACGME-accredited residency programs and 49 non-ACGME programs, has served as GME director for 28 of his 33 years at Duke. It took a three-ring binder to contain all of the letters of recommendation that people from Duke and other institutions wrote to the awards committee. In these letters, they describe how Weinerth fulfills the award requirements: dedication to promoting the professional, ethical, and personal development of residents and commitment to safe and appropriate care of patients.

Every October 6, Duke University Medical Center takes a moment to celebrate its history as the birthplace of the physician assistant (PA) profession, recognize the graduation day of its inaugural class of PAs in 1967, and honor the birthday of **Eugene Stead Jr., MD**, who pioneered the PA program during his tenure as the chair of the Duke Department of Medicine.

Duke's PA Week festivities included a ceremony attended by **R. Sanders Williams, MD**, dean of the School of Medicine, **E. Harvey Estes Jr., MD**, one of founders of the PA profession, and **Lloyd Michener, MD**, chairman of the Department of Community and Family Medicine.

As part of the celebration, the following PAs and former PA faculty members were inducted into the Duke PA Hall of Fame:

- **Lovest Alexander Jr., MHS, PA-C**
- **James Schmidt, BHS, PA-C**
- **Lisa Shock, MHS, PA-C**
- **Margaret Schmidt, EdD, CLS**
- **Roger Whittaker, BS, PA** (posthumous)

Doug Borg, director of risk management for Duke University Medical Center, was chosen as president-elect of the National American Society for Healthcare Risk Management.

Society initiatives focus on developing and implementing safe and effective patient care practices, the preservation of financial resources, and the maintenance of safe working environments.

Scott Cousins, MD, the Robert Machemer Professor of Ophthalmology and director of the Duke Center for Macular Diseases, has received a prestigious Alcon Research Institute Award. The $100,000 award will support the research of young scientists and new recruits in Duke's Center for Macular Diseases.

Former School of Nursing Dean **Ruby Wilson, EdD, RN**, received the University Medal for Distinguished Meritorious Service, one of the university's highest awards.

Wilson, a professor of nursing, assistant professor of medicine, and assistant to the chancellor for health affairs, came to Duke's nursing school in 1955 as a young faculty member. She helped develop a pioneering undergraduate curriculum and graduate nursing program, serving as the school's dean from 1971 to 1984.

Darell Bigner, MD, PhD, director of the Preston Robert Tisch Brain Tumor Center at Duke, received the honorary degree of doctor of medicine at Lund University in Sweden.

The honorary degree is given to a prominent scientist who has collaborated with the university. During the three-hour ceremony conducted in Latin, Bigner was honored for his career-long contributions to brain tumor research and for his longstanding collaboration with Swedish investigators.

Bigner is also an Edwin L. Jones Jr. and Lucille Finch Jones Cancer Research Professor and director of the Pediatric Brain Tumor Foundation Institute at Duke.

Victoria Seewaldt, MD, associate professor of medical oncology, cancer biology, and pharmacology and director of Duke's Breast Wellness Clinic, has received the annual Medical Achievement Award from the Avon-National Cancer Institute Progress for Patients program.

Seewaldt and her research team have been instrumental in coupling a new test, Random Periareolar Fine Needle Aspiration, with sensitive new molecular tests. The tests enable researchers to test breast cells for specific molecular changes that may precede breast cancers and help women track whether they are responding to preventive agents.

Doug Vinsel, CEO of Duke Raleigh Hospital, was named a board member of the Alice Aycock Poe Center for Health Education. The center is a statewide, nonprofit organization committed to healthy lifestyle education for all youth in North Carolina. **Rick Gannotta**, the hospital's COO, was named to the boards of directors of Urban Ministries and of HOSPAC, the political action committee for the North Carolina Hospital Association.

Gillian Sanders, PhD, a medical decision analyst at the Duke Clinical Research Institute, has been named president-elect of the Society for Medical Decision Making. The goal of the national organization is to improve health outcomes by providing a national forum that connects and educates researchers, health care providers, policymakers, and the public.

ANESTHESIOLOGY

Michael L. James, MD
Particular Clinical Interests and Skills: Neurocritical care unit, neuroanesthesia for neurosurgical procedures including craniotomy, deep brain stimulation, multi-level back and neck surgery, and endovascular repair; research interests in intracerebral hemorrhage including mouse modeling and developing strategies for intraoperative neural monitoring
Faculty Rank: Assistant Professor
Division: Anesthesiology
MD Degree: Louisiana State University School of Medicine, 1999
Residency: Internal Medicine, Duke University Medical Center, 2000
Neurology, Duke University Medical Center, 2003
Anesthesiology, Duke University Medical Center, 2006
Fellowship: Neurocritical Care, Duke University Medical Center, 2006

Cheryl A. Jones, MD
Particular Clinical Interests and Skills: Women's anesthesia
Faculty Rank: Assistant Professor
Division: Anesthesiology
MD Degree: University of Connecticut School of Medicine, 2002
Residency: Anesthesiology, Duke University Medical Center, 2006

COMMUNITY AND FAMILY MEDICINE

Natalie L. Fowler, MD
Particular Clinical Interests and Skills: Family medicine including women's health, adolescent medicine, preventative medicine, and chronic disease management
Faculty Rank: Clinical Associate
Division: Family Medicine
MD Degree: Washington University in St. Louis School of Medicine, 2000
Residency: Family Medicine, MetroHealth Medical Center, Cleveland, 2003

Viviana Martinez-Bianchi, MD
Particular Clinical Interests and Skills: Full scope of family medicine, health promotion, care to immigrant populations, community health, health care disparities, Latino health care, care for underserved populations
Faculty Rank: Assistant Clinical Professor
Division: Family Medicine
MD Degree: Universidad Nacional de Rosario, Argentina, 1990
Residency: Family Medicine, Hinsdale, Illinois, 1992-1994
Family Medicine, University of Iowa Hospitals and Clinics, 1994-1996
Faculty Development with Emphasis In Caring For Minorities and Underserved Populations, University of Cincinnati, 2006

Harry C. Stafford, MD
Particular Clinical Interests and Skills: Non-operative orthopaedic care, diabetes, and athletics, general family medicine, primary care sports medicine
Faculty Rank: Clinical Associate
Division: Family Medicine
MD Degree: University of North Carolina at Chapel Hill School of Medicine, 2002
Residency: Family Medicine, Duke University Medical Center, 2005
Fellowship: Primary Care Sports Medicine, Duke University Medical Center, 2006

Gloria M. Trujillo, MD
Particular Clinical Interests and Skills: Pediatrics, sports medicine, alternative medicine including acupuncture; preventative health maintenance including chronic disease management
Faculty Rank: Clinical Associate
Division: Family Medicine
MD Degree: George Washington University School of Medicine, Washington, DC, 1992
Residency: Family Medicine, Fairfax Family Practice Centers, Medical College of Virginia, 1995

DUKE UNIVERSITY AFFILIATED PHYSICIANS

Jennifer L. Eaton, MD
Particular Clinical Interests and Skills: Urgent care medicine, patients of all ages, community health promotion, access to care for the underserved
Faculty Rank: Consulting Associate
Division: Duke Urgent Care
MD Degree: University of North Carolina at Chapel Hill School of Medicine, 2003
Residency: Emergency Medicine, UNC Hospitals, 2003-2006
Other Degree: MPH, Health Behavior/Health Education, University of North Carolina at Chapel Hill, 1999

Anita M. Pisharody, MD
Particular Clinical Interests and Skills: Women's health, family counseling, adolescent counseling, and discussion of parenting issues
Faculty Rank: Consulting Associate
Division: Triangle Family Practice
MD Degree: NRS Medical College, University of Calcutta, India, 1990
Residency: Rotating Internship, NRS Medical College, University of Calcutta, India, 1990-1991
OB/GYN, NRS Medical College, University of Calcutta, India, 1991-1992
Family Practice, Methodist Medical Center, Illinois, 1995-1998

Allen T. Smith, MD
Particular Clinical Interests and Skills: Primary and preventative health care for children and adults, musculoskeletal problems, sports medicine, chronic illness management
Faculty Rank: Consulting Associate
Division: Butner-Creedmoor Family Medicine
MD Degree: Uniformed Services University of the Health Sciences, Maryland, 1983
Residency: Family Medicine, Malcolm Grow Medical Center, Maryland, 1983-1986

Roberts H. Smith, MD
Particular Clinical Interests and Skills: Urgent care
Faculty Rank: Clinical Associate
Division: Duke Urgent Care
MD Degree: University of Texas Medical School at Houston, 1990
Residency: Internal Medicine/Pediatrics, Duke University Medical Center, 1990-1994
Other Degree: MS, University of Texas - Houston, 1990

May A. Thomas, MD
Particular Clinical Interests and Skills: Geriatric primary care with comprehensive geriatric assessment, preventative medicine and health maintenance in internal medicine and geriatrics
Faculty Rank: Consulting Associate
Division: Metropolitan Durham Medical Group
MD Degree: Temple University School of Medicine, Philadelphia, 1981
Residency: Internal Medicine, Graduate Hospital, Philadelphia, 1981-1984

MEDICINE

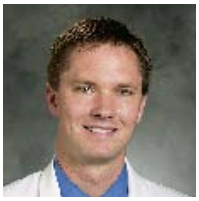
Manal Abdelmalek, MD
Particular Clinical Interests and Skills: Obesity-related liver disease and the metabolic syndrome of insulin resistance including evaluation of new treatment options and examining the impact of fatty liver from a public health perspective
Faculty Rank: Associate Professor
Division: Gastroenterology
MD Degree: University of Missouri-Kansas City School of Medicine, 1992
Residency: Internal Medicine, Mayo Clinic, Minnesota, 1992-1995
Fellowship: Gastroenterology/ Hepatology, Mayo Clinic, Arizona and Minnesota, 1995-1998
Other Degree: MPH, University of Florida, 2004

Andrew J. Armstrong, MD
Particular Clinical Interests and Skills: Drug development and novel strategies for the treatment and management of advanced prostate cancer and other GU malignancies, targeted therapy, mTOR/Akt pathway inhibitor; prognostic and surrogate models in GU malignancies, perioperative biologic therapeutics
Faculty Rank: Assistant Professor
Division: Medical Oncology
MD Degree: University of Virginia School of Medicine, 2000
Residency: Internal Medicine, Hospital of the University of Pennsylvania, 2000-2003
Fellowship: Medical Oncology, Johns Hopkins University, Maryland, 2003-2006
Other Degrees: BSE, Duke University Pratt School of Engineering
MSc, Johns Hopkins School of Public Health, Maryland, pending 2007

Carla W. Brady, MD
Particular Clinical Interests and Skills: General and transplant hepatology
Faculty Rank: Associate
Division: Gastroenterology
MD Degree: University of Virginia School of Medicine, 1997
Residency: Internal Medicine, Drexel University College of Medicine, Philadelphia, 2001
Fellowship: Gastroenterology, Drexel University College of Medicine, Philadelphia, 2005
Other Degree: MHS, Duke University, 2006

Vivian H. Chu, MD
Particular Clinical Interests and Skills: Staphylococcal infections, endocarditis, osteomyelitis, prosthesis-related infections, general infectious diseases, HIV
Faculty Rank: Associate
Division: Infectious Diseases and International Health
MD Degree: Columbia University College of Physicians and Surgeons, New York City, 2000
Residency: Internal Medicine, Duke University Medical Center, 2000-2003
Fellowship: Infectious Diseases, Duke University Medical Center, 2003-2006
Other Degree: MHS, Duke University, 2005

Jerry Evans, MD
Particular Clinical Interests and Skills: Advanced biliary endoscopy, advanced imaging techniques, and therapeutic general endoscopy
Faculty Rank: Assistant Professor
Division: Gastroenterology
MD Degree: University of Tennessee Graduate School of Medicine, 1998
Residency: Internal Medicine, Emory University Woodruff Health Sciences Center, Atlanta, 2001
Fellowship: Gastroenterology, Massachusetts General Hospital, Boston, 2005
Advanced Biliary and Therapeutic Endoscopy, Hospital of the University of Pennsylvania, 2006
Other Degree: MMS, Harvard Medical School, Massachusetts, 2005



William L. Fangman, MD
Particular Clinical Interests and Skills: General dermatology, dermatopathology, pigmented lesion clinic, procedural dermatology, laser surgery
Faculty Rank: Assistant Clinical Professor
Division: Dermatology
MD Degree: University of North Carolina at Chapel Hill School of Medicine, 2001
Residency: Internal Medicine, UNC Hospitals, 2001-2002
Dermatology, Duke University Medical Center, 2002-2005
Fellowship: Dermatopathology, New York University Medical Center, 2005-2006

David M. Gallagher, MD, Durham Regional Hospitalist Program Medical Director
Particular Clinical Interests and Skills: Inpatient hospitalist medicine and hospitalist medicine leadership
Faculty Rank: Assistant Clinical Professor
Division: General Internal Medicine
MD Degree: George Washington University School of Medicine, Washington, DC, 1990
Residency: Internal Medicine, University of California, San Francisco Medical Center, 1993-1996
Anatomic and Clinical Pathology, University of California, San Francisco Medical Center, 1990-1993

Charles William "Bill" Hargett III, MD
Particular Clinical Interests and Skills: Pulmonary vascular disease (pulmonary hypertension and pulmonary embolism), critical care medicine
Faculty Rank: Associate
Division: Pulmonary, Allergy, and Critical Care
MD Degree: University of Virginia School of Medicine, 1999
Residency: Internal Medicine, Duke University Medical Center, 1999-2003
Fellowship: Pulmonary, Allergy, and Critical Care Medicine, Duke University Medical Center, 2003-2006

S. Nicole Hastings, MD
Particular Clinical Interests and Skills: Comprehensive geriatric assessment, medication use in the elderly, transitions of care and care coordination
Faculty Rank: Associate
Division: Geriatrics
MD Degree: University of North Carolina at Chapel Hill School of Medicine, 1998
Residency: Internal Medicine, Stanford University Medical Center, California, 1998-2001
Fellowship: Geriatric Medicine, Duke University Medical Center, 2003-2006

Edward F. Hendershot, MD
Particular Clinical Interests and Skills: General infectious diseases, prosthetic joint infections, tuberculosis
Faculty Rank: Assistant Professor
Division: Infectious Diseases and International Health
MD Degree: University of Louisville School of Medicine, Kentucky, 1985
Residency: Internal Medicine, Emory University Woodruff Health Sciences Center, Atlanta, 1988
Fellowship: Infectious Diseases, Emory University Woodruff Health Sciences Center, Atlanta, 1991

Yuh-Chin Tony Huang, MD
Particular Clinical Interests and Skills: Asthma, COPD, sepsis, pulmonary hypertension, hereditary hemorrhagic telengiectasia
Faculty Rank: Professor
Division: Pulmonary, Allergy, and Critical Care
MD Degree: National Taiwan University College of Medicine, 1983
Residency: Medicine, Maryland General Hospital, 1988
Fellowship: Pulmonary and Critical Care Medicine, Duke University Medical Center, 1991
Other Degree: MHS, Environmental Health Sciences, Johns Hopkins University, Maryland, 1984

MEDICINE

Paul W. Noble, MD
Particular Clinical Interests and Skills: Pulmonary, allergy, and critical care
Faculty Rank: Professor
Division: Pulmonary, Allergy, and Critical Care
MD Degree: New York University School of Medicine, 1984
Residency: Internal Medicine, University of California, San Francisco Medical Center, 1988
Fellowship: Pulmonary Program, University of Colorado Health Sciences Center, 1991

Manesh R. Patel, MD
Particular Clinical Interests and Skills: Diagnostic and interventional coronary angiography and peripheral angiography and percutaneous intervention, cardiac MRI, clinical trials in patients with coronary artery disease and cardiac imaging
Faculty Rank: Assistant Professor
Division: Cardiology
MD Degree: Emory University School of Medicine, Atlanta, 1997
Residency: Internal Medicine, Duke University Medical Center, 2000
Chief Resident, Duke University Medical Center, 2001-2002
Fellowship: Cardiology, Duke University Medical Center, 2005
Interventional Cardiology, Duke University Medical Center, 2006

Patrick A. O'Connell, MD
Particular Clinical Interests and Skills: General internal medicine
Faculty Rank: Consulting Associate
Division: General Internal Medicine
MD Degree: University of North Carolina at Chapel Hill School of Medicine, 2000
Residency: Internal Medicine, Johns Hopkins Bayview Medical Center, Maryland, 2003
Assistant Chief of Service, Johns Hopkins Bayview Medical Center, Maryland, 2003-2004

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Sylver Quevedo, MD
Duke Integrative Medicine Medical Director
Particular Clinical Interests and Skills: Integrative medicine, quality of life in chronic illness
Division: Nephrology
MD Degree: Harvard Medical School, 1975
Residency: Family Medicine, University of Arizona Health Sciences Center, 1976; Internal Medicine, Santa Clara Valley Medical Center/ Stanford Hospital & Clinics, 1985
Fellowship: Nephrology and Medicine, Stanford University Hospital & Clinics, 1988; Robert Wood Johnson Clinical Scholar, Stanford University School of Medicine, 1985-1987
Other: MPH, Harvard School of Public Health, 1975

Donald M. Rabil, MD
Particular Clinical Interests and Skills: Cough, dyspnea, COPD, asthma, lung cancer, sarcoid, interstitial lung disease, pleural disease, occupational lung disease
Faculty Rank: Consulting Associate
Division: Pulmonary, Allergy, and Critical Care
MD Degree: Brody School of Medicine at East Carolina University, North Carolina, 1983
Residency: Internal Medicine, Pitt County Memorial Hospital, ECU School of Medicine, North Carolina, 1983-1986
Fellowship: Pulmonary Diseases, University of Virginia Medical Center, 1986-1988

Kaushik Sen, MD
Particular Clinical Interests and Skills: Medical oncology as well as benign and malignant hematology patients, research interest in head and neck malignancies
Faculty Rank: Assistant Professor
Division: Medical Oncology
MD Degree: MD, Calcutta National Medical College, India, 1989
MD in Internal Medicine and Hematology (equivalent to Fellowship), Institute of Postgraduate Medical Education and Research, India, 1990
Residency: Internal Medicine, University of North Dakota, 1997
Fellowship: Medical Oncology, Cleveland Clinic, 2002

Ajay K. Shukla, MD
Particular Clinical Interests and Skills: Neuromuscular disorders, peripheral neuropathies, Botox treatment for spasticity and in related areas, epilepsy, epilepsy monitoring, EMG, and nerve conduction studies, general neurology including headaches, stroke
Faculty Rank: Consulting Associate
Division: Neurology
MD Degree: Maulana Azad Medical College, New Delhi, 1990
Residency: Internal Medicine, University of Missouri-Columbia Health Care, 2001-2002
Neurology, University of Missouri-Columbia Health Care, 2002-2005
Fellowship: Clinical Neurophysiology, Vanderbilt Medical Center, Tennessee, 2005-2006

Tracy L. Setji, MD
Particular Clinical Interests and Skills: Polycystic ovary syndrome, women's health, hirsutism, general endocrinology, diabetes including diabetes in pregnancy, thyroid disorders, pituitary disease, and osteoporosis
Faculty Rank: Associate
Division: Endocrinology, Metabolism, and Nutrition
MD Degree: University of Arizona College of Medicine, 2000
Residency: Internal Medicine, University Medical Center, Arizona, 2000-2003
Fellowship: Endocrinology, Diabetes and Metabolism, Duke University Medical Center, 2003-2006

Melissa Teitelman, MD
Particular Clinical Interests and Skills: Gastroenterology
Faculty Rank: Assistant Clinical Professor
Division: Gastroenterology
MD Degree: Temple University School of Medicine, Philadelphia
Residency: Internal Medicine, Duke University Medical Center, 1999-2002
Fellowship: Gastroenterology, Hospital of the University of Pennsylvania, 2003-2006
Other Degree: MS, Clinical Epidemiology, University of Pennsylvania, 2006

Jaspal Singh, MD
Particular Clinical Interests and Skills: Critical illness and the effects of obesity on critical illness, studying the effects of the environment on asthma and the genetic makeup of environmental asthma
Faculty Rank: Assistant Clinical Professor
Division: Pulmonary, Allergy, and Critical Care
MD Degree: University of Illinois College of Medicine at Chicago, 1999
Residency: Internal Medicine, University of Rochester Medical Center, New York, 1999-2002
Fellowship: Pulmonary and Critical Care, Duke University Medical Center, 2003-2006
Other Degree: MHS, Duke University, 2006

Neil L. Spector, MD
Particular Clinical Interests and Skills: Development of experimental therapeutics for solid and hematological malignancies
Faculty Rank: Associate Professor
Division: Medical Oncology
MD Degree: University of Medicine & Dentistry of New Jersey, 1982
Residency: Internal Medicine, Parkland Hospital, University of Texas Southwestern Medical Center, 1982-1986
Fellowship: Medical Oncology and Hematology, Harvard Medical School, Massachusetts, 1986-1989

Jane V. Trinh, MD
Particular Clinical Interests and Skills: General internal medicine and pediatric medicine, chronic disease management, transition medicine management of chronic childhood diseases into adulthood
Faculty Rank: Clinical Associate
Division: General Internal Medicine
MD Degree: Duke University School of Medicine, 2002
Residency: Combined Internal Medicine and Pediatrics, Duke University Medical Center, 2002-2006

ON THE SPOT

Q. How is integrative medicine best defined today?

A. Integrative medicine is often mistakenly used interchangeably with "complementary medicine" or "alternative medicine." Integrative medicine is much more; it strongly emphasizes the very best of conventional medicine, cutting-edge diagnosis, and treatment with appropriate complementary therapies. Whenever possible, the practice favors the use of low-tech, low-cost interventions. All factors that affect health, wellness, and disease are considered, including the psychosocial and spiritual dimensions of a person's life. It brings patients and caregivers into a partnership to achieve the patient's optimal health and healing.

—Sylver Quevedo, MD

OPHTHALMOLOGY

Philip E. Wakefield, MD
Particular Clinical Interests and Skills: Tropical dermatology including leprosy
Faculty Rank: Assistant Clinical Professor
Division: Dermatology
MD Degree: University of Virginia School of Medicine, 1984
Residency: Dermatology, Walter Reed Army Medical Center, Washington, DC, 1988-1991

Heather E. Whitson, MD
Particular Clinical Interests and Skills: Geriatrics and particularly multimorbidity (the accumulation of diseases and conditions), frailty, functional decline
Faculty Rank: Associate
Division: Geriatrics
MD Degree: Weill Medical College of Cornell University, New York City, 2000
Residency: Internal Medicine, Duke University Medical Center, 2003
Fellowship: Geriatrics, Duke University Medical Center, 2006

Parag D. Gandhi, MD
Particular Clinical Interests and Skills: Aesthetic and reconstructive surgery of the face and eyelids, tear duct surgery—adult and pediatric, tumor surgery of the lids and orbit, thyroid eye disease and orbital decompression, Botox and fillers, laser skin resurfacing
Faculty Rank: Assistant Consulting Professor
Division: Oculoplastic and Reconstructive Service
MD Degree: Mount Sinai School of Medicine, New York City, 2000
Residency: Ophthalmology, The Mount Sinai Hospital, New York City, 2004
Fellowship: Ophthalmic Plastic and Reconstructive Surgery, University of Tennessee Hamilton Eye Institute and Vanderbilt University Eye Institute, 2006

Aaleya F. Koreishi, MD
Particular Clinical Interests and Skills: General and urgent eye care, cataract surgery, intraocular lens implantation, dry eyes, cornea, and external disease
Faculty Rank: Assistant Clinical Professor
Division: Comprehensive Ophthalmology Service
MD Degree: University of Michigan Medical School, 2000
Residency: Ophthalmology, Wilmer Eye Institute, Johns Hopkins Hospital, Maryland, 2001-2004
Fellowship: Cornea and External Disease, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Florida, 2004-2005

Jill B. Koury, MD
Particular Clinical Interests and Skills: Comprehensive ophthalmology
Faculty Rank: Assistant Clinical Professor
Division: Comprehensive Ophthalmology Service
MD Degree: Tulane University School of Medicine, New Orleans, 1981
Residency: Ophthalmology, Ochsner Medical Foundation, Louisiana, 1981-1983
Fellowship: Glaucoma, Ochsner Medical Foundation/Louisiana State University Eye Center, 1984

Molly M. Walsh, MD
Particular Clinical Interests and Skills: Medical, laser and surgical management of various types of glaucoma, including open angle, uveitic and pigmentary glaucoma, cataract surgery, treatment of dry eye, and diabetic eye disease
Faculty Rank: Assistant Professor
Division: Glaucoma Service
MD Degree: Tulane University School of Medicine, New Orleans, 2000
Residency: Tulane University Hospital & Clinic, New Orleans, 2001-2004
Fellowship: Glaucoma, Duke University Medical Center, 2004-2006
Other Degree: MPH, Glaucoma, Duke University Medical Center, 2004-2006

PATHOLOGY

Sarah M. Bean, MD
Particular Clinical Interests and Skills: Pathology, surgical pathology, cytopathology, gynecologic, and breast pathology
Faculty Rank: Assistant Professor
Division: Pathology
MD Degree: University of Rochester School of Medicine & Dentistry, New York, 2002
Residency: University of Alabama at Birmingham Medical Center, 2006
Fellowship: Cytopathology, University of Alabama at Birmingham Medical Center, 2005

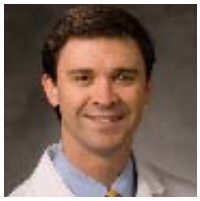
Shannon J. McCall, MD
Particular Clinical Interests and Skills: Anatomic pathology services including intra-operative tissue evaluation as well as routine specimen reports, gastrointestinal and liver pathology
Faculty Rank: Assistant Professor
Division: Pathology
MD Degree: Duke University School of Medicine, 2000
Residency: Anatomical and Clinical Pathology, Duke University Medical Center, 2000-2004
Fellowship: Gastrointestinal and Hepatic Pathology, Duke University Medical Center, 2004-2005

PEDIATRICS

Stacy P. Ardoin, MD
919-684-6575
Particular Clinical Interests and Skills: Pediatric rheumatic conditions, adult rheumatic conditions, systemic lupus erythematosus, vasculitis, inflammatory arthritis, rheumatoid arthritis
Faculty Rank: Clinical Associate
Division: Rheumatology
MD Degree: The Ohio State University College of Medicine, 1997
Residency: Internal Medicine and Pediatrics, The Ohio State University Medical Center, 1997-2001
Internal Medicine Chief Residency, The Ohio State University Medical Center, 2001-2002
Fellowship: Adult and Pediatric Rheumatology, Duke University Medical Center, 2002-2006

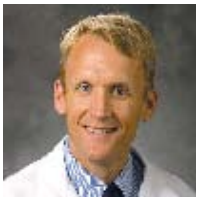
Evelyn M. Artz, MD
919-684-3772
Particular Clinical Interests and Skills: General pediatric endocrinology including type 1 diabetes, celiac disease and type 1 diabetes, disorders of pubertal development, growth, thyroid dysfunction, and hypothalamic pituitary dysfunction
Faculty Rank: Instructor
Division: Endocrinology and Diabetes
MD Degree: Louisiana State University School of Medicine, 1998
Residency: Pediatrics, University of California, Irvine Medical Center, 1998-2002
Fellowship: Pediatric Endocrinology, Duke University Medical Center, 2003-2006

Kamlesh V. Athavale, MD
Particular Clinical Interests and Skills: Neonatal-perinatal medicine
Faculty Rank: Associate Professor
Division: Neonatal-Perinatal Medicine
MD Degree: MBBS, University of Mumbai, India, 1993
MD, Pediatrics, University of Mumbai, India, 1997
Residency: Pediatrics, University of Mumbai, India, 1994-1997
Pediatrics, Miami Children's Hospital, Florida, 2002-2004
Fellowship: Neonatal-Perinatal Medicine, Jackson Memorial Hospital, Miami, 1999-2001



Jeremy S. Baker, MD
Particular Clinical Interests and Skills: Care of infants, children, and young adults
Faculty Rank: Clinical Associate
Division: Children's Primary Care
MD Degree: University of Florida College of Medicine, 2002
Residency: Pediatrics, Duke University Medical Center, 2002-2006

RADIATION ONCOLOGY

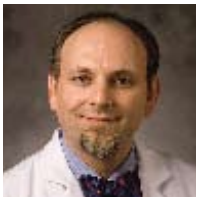


Robert W. Benjamin, MD
Particular Clinical Interests and Skills: Disorders of calcium and phosphorus metabolism, disorders of sexual differentiation, and congenital adrenal hyperplasia
Faculty Rank: Clinical Associate
Division: Endocrinology
MD Degree: Medical College of Georgia School of Medicine, 2000
Residency: Pediatrics, University of Wisconsin Hospitals and Clinics, 2003
Fellowship: Pediatric Endocrinology, UNC Hospitals, 2006

William B. Gallentine, DO
Particular Clinical Interests and Skills: Most pediatric neurological problems, special interests include epilepsy, neurodegenerative, neurometabolic, and neuromuscular disorders
Faculty Rank: Associate
Division: Neurology
DO Degree: Philadelphia College of Osteopathic Medicine, 2000
Residency: Pediatrics, Geisinger Medical Center, Pennsylvania, 2000-2003
Fellowship: Pediatric Neurology, Duke University Medical Center, 2003-2006

M. Susan LaTuga, MD
Particular Clinical Interests and Skills: Neonatal-perinatal medicine
Faculty Rank: Clinical Associate
Division: Neonatal-Perinatal Medicine
MD Degree: University of North Carolina at Chapel Hill School of Medicine, 2001
Residency: Pediatrics, The Children's Hospital at Montefiore, New York City, 2004
Other Degree: MPH, Maternal and Child Health, UNC School of Public Health, 2000

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, Baltimore, 1990
Fellowship: Pediatric Cardiology, Children's Hospital Boston, 1994
Medical Genetics, University of Michigan Taubman Health Care Center, 2003



Xavier A. Preud'homme, MD
Particular Clinical Interests and Skills: Inpatient care for patients with active internal medicine and psychiatric comorbidities (med-psych), electroconvulsivotherapy (ECT), sleep research
Faculty Rank: Assistant Professor
Division: Biological Psychiatry
MD Degree: Universite Libre de Bruxelles Faculty of Medicine, Belgium, 1993
Residency: Psychiatry, Universite Libre de Bruxelles, Belgium, 1998
Psychiatry, Duke University Medical Center, 2006
Internal Medicine, Duke University Medical Center, 2006

Mohit S. Kasibhatla, MD
Particular Clinical Interests and Skills: Radiotherapy of head and neck and gynecologic malignancies, clinical trials in head and neck and gynecologic malignancies, image-guided radiotherapy
Faculty Rank: Associate
Division: Radiation Oncology
MD Degree: Duke University School of Medicine, 2000
Residency: Internal Medicine, Hospital of the University of Pennsylvania, 2001
Radiation Oncology, Duke University Medical Center, 2001-2005

Jeffrey M. Ferranti, MD
Particular Clinical Interests and Skills: Medical informatics, computerized patient safety initiatives, quality improvement metrics, electronic research data exchange, medical data standards and interoperability, neonatal critical care, CPOE, electronic medical records
Faculty Rank: Clinical Associate
Division: Neonatal-Perinatal Medicine
MD Degree: McGill University Faculty of Medicine, Montreal, 2000
Residency: Pediatrics, Duke University Medical Center, 2003
Fellowship: Neonatology, Duke University Medical Center, 2006
Other Degree: MS, Duke University, 2006

Mary E. Hartman, MD
Particular Clinical Interests and Skills: Pediatric critical care medicine
Faculty Rank: Associate
Division: Critical Care Medicine
MD Degree: University of Rochester School of Medicine & Dentistry, New York, 1999
Residency: Pediatrics, Golisano Children's Hospital at Strong, New York, 1999-2002
Fellowship: Pediatric Critical Care Medicine, Children's Hospital of Pittsburgh, 2002-2006
Other Degree: MPH, University of Pittsburgh, 2006

M. Anthony Moody, MD
Particular Clinical Interests and Skills: General pediatric infectious diseases, pediatric tuberculosis, sexually transmitted infections
Faculty Rank: Associate
Division: Infectious Diseases
MD Degree: Duke University School of Medicine, 1999
Residency: Categorical Pediatrics, Emory University Woodruff Health Sciences Center, Atlanta, 1999-2002
Pediatrics, Chief Resident, Emory University Woodruff Health Sciences Center, Atlanta, 2002-2003
Fellowship: Pediatric Infectious Diseases, Duke University Medical Center, 2003-2006

PSYCHIATRY

Margaret Maytan, MD
Particular Clinical Interests and Skills: Psycho-oncology, end-of-life care, anxiety and depression, mind-body medicine
Faculty Rank: Clinical Associate
Division: Outpatient Psychiatry
MD Degree: Umeå University Faculty of Medicine, Sweden, 1996
Residency: Psychiatry, Duke University Medical Center, 2006
Other Degree: MA, Musicology, University of North Carolina at Chapel Hill, 1976

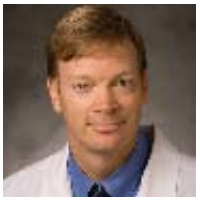
Sarah K. Rivelli, MD
Particular Clinical Interests and Skills: General internal medicine, general psychiatry, hospitalist medicine, consultation-liaison psychiatry, delirium, affective disorders, psychosomatic medicine
Faculty Rank: Clinical Associate
Division: Biological Psychiatry
MD Degree: Universite Libre de Bruxelles Faculty of Medicine, Belgium
Residency: Internal Medicine and Psychiatry, Duke University Medical Center, 2006

W. Robert Lee, MD
Particular Clinical Interests and Skills: Treatment of genitourinary cancers (prostate, bladder) with radiotherapy, prostate brachytherapy, and intensity-modulated radiation therapy
Faculty Rank: Professor
Division: Radiation Oncology
MD Degree: University of Virginia School of Medicine, 1989
Residency: Radiation Oncology, University of Florida Health Science Center, 1993
Other Degrees: MS, Clinical Epidemiology, Wake Forest University, North Carolina, 2000
MAEd, Adult Education, Penn State University, 2006

RADIOLOGY

Daniel T. Boll, MD
Particular Clinical Interests and Skills: Abdominal imaging
Faculty Rank: Assistant Professor
Division: Abdominal Imaging
MD Degree: University of Duisburg-Essen Faculty of Medicine, Germany, 1998
Residency: Specialty, University of Ulm, Germany, 1999-2001 Specialty, University of Ulm, Germany, 2004-2006
Fellowship: MRI, Case Western Reserve University, Ohio, 2002-2003

Robert F. Bowerman, MD, PhD
Particular Clinical Interests and Skills: Diagnostic radiology
Faculty Rank: Consulting Associate
Division: Community Radiology
MD Degree: University of Miami Miller School of Medicine, Florida, 1983
Residency: Specialty, University of Kansas Medical Center, 1987
Other Degree: PhD, Neurosciences, University of Miami, Florida, 1971



Charles M. Maxfield, MD
Particular Clinical Interests and Skills: Pediatric radiology
Faculty Rank: Associate Clinical Professor
Division: Pediatric Radiology
MD Degree: Dartmouth Medical School, New Hampshire, 1988
Residency: Radiology, Duke University Medical Center, 1989-1993
Fellowship: Pediatric Radiology, Duke University Medical Center, 1993-1994

Sora C. Yoon, MD
Particular Clinical Interests and Skills: Radiology
Faculty Rank: Associate
Division: Breast Imaging
MD Degree: New York University School of Medicine, 2000
Residency: Diagnostic Radiology, New York-Presbyterian Hospital/Weill Cornell Medical Center
Fellowship: Breast Imaging, UNC Hospitals

SURGERY

Randall M. Best, MD
Particular Clinical Interests and Skills: Clinical practice at emergency medicine coupled with medical-legal issues including medical malpractice and regulatory law
Faculty Rank: Assistant Professor
Division: Emergency Medicine
MD Degree: University of North Carolina at Chapel Hill School of Medicine, 1981
Residency: Emergency Medicine, Henry Ford Hospital, Detroit, 1984

Gregory D. Bianchi, MD
Particular Clinical Interests and Skills: Prostate disease, stone disease, erectile dysfunction, female urinary incontinence, no-scalpel vasectomy, endourology, laparascopy, general urology
Faculty Rank: Assistant Clinical Professor
Division: Urology
MD Degree: MD, Rush Medical College, Chicago, 1994
Residency: Urology, University of Iowa Hospitals & Clinics, 2000
Fellowship: Endo-urology and Laparoscopy, University of Cincinnati Academic Health Center, 2006
Other Degree: MS, Preventative Medicine and Environmental Health with Emphasis in Public Health, University of Iowa, 1998

Christopher R. Brown, MD
Particular Clinical Interests and Skills: Cervical radiculopathy and myelopathy as well as complex cervical reconstruction, total disc replacement, spine tumors, and degenerative conditions of the thoracic and lumbar spine
Faculty Rank: Assistant Clinical Professor
Division: Orthopaedic Surgery
MD Degree: Medical College of Virginia, 2000
Residency: Orthopaedics, Duke University Medical Center, 2005
Fellowship: Spine, Emory University Woodruff Health Sciences Center, Atlanta, 2005-2006

Seth M. Cohen, MD
Particular Clinical Interests and Skills: Adult voice, airway, and swallowing problems
Faculty Rank: Assistant Professor
Division: Otolaryngology–Head and Neck Surgery
MD Degree: University of North Carolina at Chapel Hill School of Medicine, 2000
Residency: Otolaryngology, Vanderbilt Medical Center, Tennessee, 2005
Fellowship: Laryngology, Vanderbilt Medical Center, Tennessee, 2006
Other Degree: MPH, University of North Carolina at Chapel Hill School of Public Health, 1999

Adele K. Evans, MD
Particular Clinical Interests and Skills: Pediatric hearing loss and treatment, pediatric chronic otitis media, management and coordination of pediatric multidisciplinary patients, such as cleft palate, craniofacial and cochlear implant clinics, pediatric nasal polyposis and sinus surgery, pediatric airway disorders, including perinatal airway management via EXIT procedures and treatment of chronic airway disease such as subglotticstenosis, resident education, medical student education
Faculty Rank: Assistant Professor
Division: Otolaryngology-Head and Neck Surgery
MD Degree: Emory University School of Medicine, Atlanta, 2000
Residency: General Surgery, Beth Israel Deaconess Medical Center, Boston, 2000-2001 Otolaryngology-Head and Neck Surgery, Massachusetts Eye and Ear Infirmary, 2001-2005
Fellowship: Pediatric Otolaryngology, The Children's Hospital of Philadelphia, 2005-2006

Brian R. Evans, MD
Particular Clinical Interests and Skills: General urology with a focus on minimally invasive surgery, including laparoscopy and robotics
Faculty Rank: Instructor
Division: Urology
MD Degree: Medical University of Ohio, 2000
Residency: General Surgery, Duke University Medical Center, 2000-2002
Urology, Duke University Medical Center, 2002-2006

Gerald A. Grant, MD
Particular Clinical Interests and Skills: Pediatric neurosurgery, pediatric brain tumors, pediatric epilepsy, Chiari malformation, pediatric spinal disorders
Faculty Rank: Assistant Professor
Division: Neurosurgery
MD Degree: Stanford University School of Medicine, 1994
Residency: Neurosurgery, University of Washington Medical Center, 1994-2001
Fellowship: Pediatric Neurosurgery, Children's Hospital and Regional Medical Center, Seattle, 2001-2002

Harry M. Lightfoot Jr., MD
Particular Clinical Interests and Skills: General surgery
Faculty Rank: Assistant Professor
Division: General Surgery
MD Degree: University of North Carolina School of Medicine, 1999
Residency: Surgery, UNC Hospitals, 2006

Alexander T. Limkakeng Jr., MD
Particular Clinical Interests and Skills: Adult and pediatric emergency medicine, observational medicine, acute cardiac disease
Faculty Rank: Assistant Professor
Division: Emergency Medicine
MD Degree: University of Pennsylvania School of Medicine, 2001
Residency: Emergency Medicine, Rush University Medical Center/Stroger Cook County Hospital, Chicago, 2005

Prerana N. Patel, MD
Particular Clinical Interests and Skills: Scoliosis and other pediatric spinal deformity, developmental dysplasia of the hip, pediatric foot problems, pediatric trauma, Perthes disease, pediatric sports medicine, cerebral palsy, myelodysplasia
Faculty Rank: Assistant Clinical Professor
Division: Orthopaedic Surgery
MD Degree: Duke University School of Medicine, 2000
Residency: Orthopaedic Surgery, University of Michigan Hospitals, 2001
Fellowship: Pediatric Orthopaedic Surgery and Scoliosis, Rady Children's Hospital San Diego, 2006

Troilus A. Plante, MD
Particular Clinical Interests and Skills: Sepsis biomarkers
Faculty Rank: Assistant Clinical Professor
Division: Emergency Medicine
MD Degree: University of Massachusetts Medical School, 2002
Residency: Emergency Medicine, Rhode Island Hospital, 2006

Liana Puscas, MD
Particular Clinical Interests and Skills: Maxillofacial trauma, clinical research, thyroid and parathyroid disorders
Faculty Rank: Assistant Professor
Division: Otolaryngology-Head and Neck Surgery
MD Degree: University of Miami Miller School of Medicine, Florida, 1996
Residency: Otolaryngology, University of Southern California Hospital, 2001
Fellowship: Head and Neck Cancer, Microvascular Reconstruction, Skull Base Surgery, University of California-Davis Medical Center, 2003
Other Degree: MHS, Duke University, 2007

David H. Stone, MD
Particular Clinical Interests and Skills: Stent graft and open surgical repair of abdominal aortic and thoracic aortic aneurysms, aortic dissection, carotid artery disease, percutaneous endovascular treatment of mesenteric, renovascular and lower extremity disease
Faculty Rank: Assistant Professor
Division: General Surgery
MD Degree: New York University School of Medicine, 1997
Residency: General Surgery, New York University Medical Center, 1997-2004
Fellowship: Harvard Longwood Vascular Research Fellow, Beth Israel Deaconess Medical Center, Boston, 1999-2001 Vascular and Endovascular Surgery, Massachusetts General Hospital, 2004-2006

Dean C. Taylor, MD
Particular Clinical Interests and Skills: Orthopaedic sports medicine specializing in surgery and injuries to the shoulder and knee, arthroscopic surgery of the shoulder, knee, elbow, and ankle, shoulder instability and labral tears, knee instability and ligament tears, knee articular cartilage and meniscal injuries, ACL injuries in adults and children, muscle and tendon tears (hamstring, biceps, rotator cuff, Achilles tendon, etc.), clavicle fractures
Faculty Rank: Professor
Division: Orthopaedic Surgery
MD Degree: Duke University School of Medicine, 1985
Residency: Orthopaedic Surgery, Duke University Medical Center, 1987-1991
Fellowship: John Feagin West Point Sports Medicine, Letterman Army Institute of Research, Presidio of San Francisco, California, and Keller Army Hospital, West Point, New York, 1991-1993

David C. White, MD
Particular Clinical Interests and Skills: All aspects of general thoracic surgery with a special interest in minimally invasive surgery for lung cancer as well as benign conditions
Faculty Rank: Clinical Assistant Professor
Division: Cardiovascular and Thoracic Surgery
MD Degree: University of Virginia School of Medicine, 1996
Residency: General Surgery, Duke University Medical Center, 1996-2003
Fellowship: Thoracic Surgery, Duke University Medical Center, 2003-2006

Search Duke's comprehensive Physician Referral Directory online at dukehealth.org/physician_search

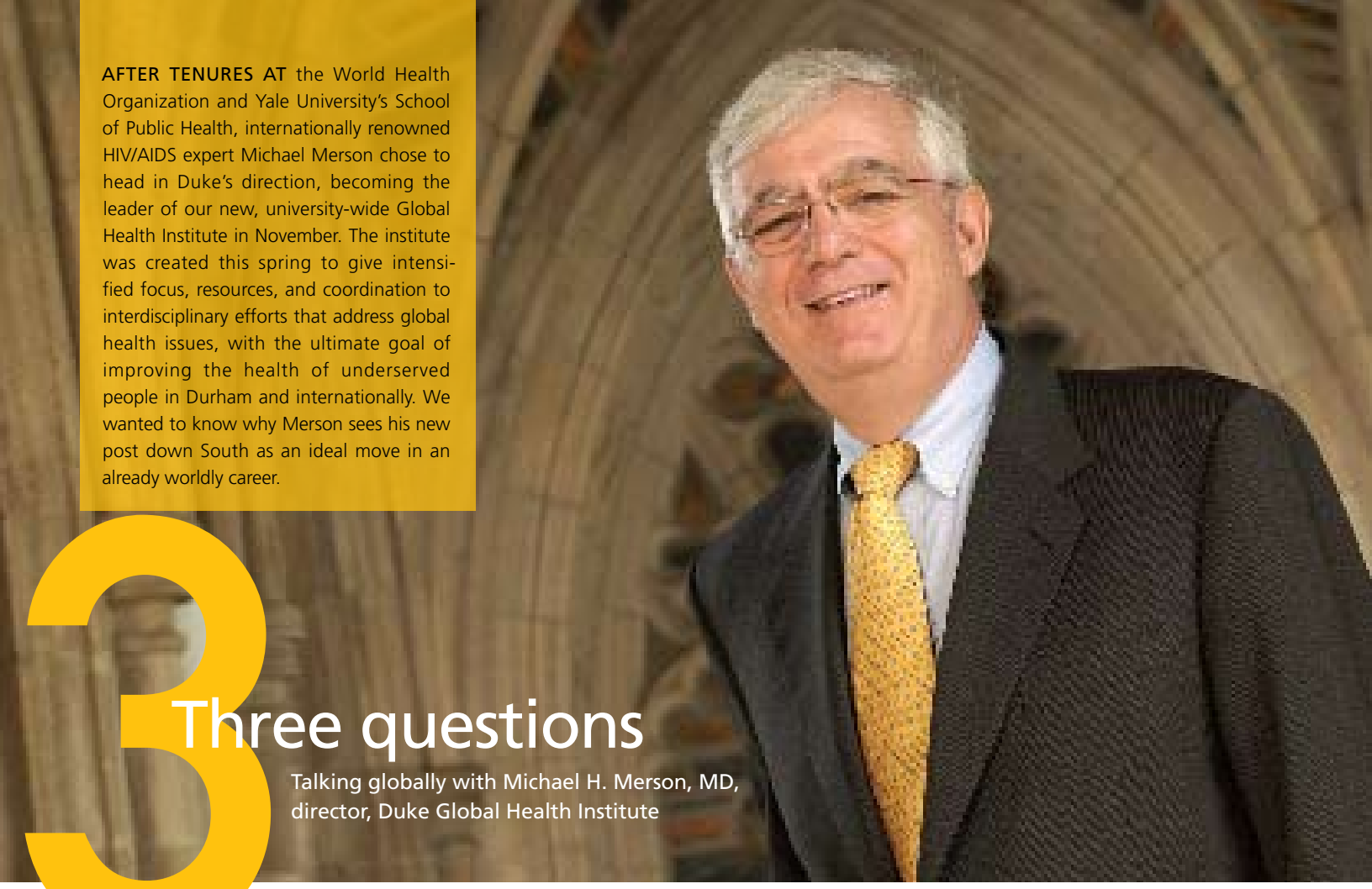
ON THE SPOT

Q. What steps can be taken to improve recovery after knee surgery?

A. Over the last 25 years we have made great advancements in reducing recovery time following knee surgery. The development of arthroscopy has been one of the greatest advances in orthopaedic surgery. Arthroscopic procedures for many joints—and especially in the knee—result in smaller incisions and less painful procedures with more rapid return to activity.

Advances in physical therapy have also led to more rapid recovery following knee surgery. Research has demonstrated that rehabilitation focusing on early motion and early functional return results in better outcomes than older techniques emphasizing immobilization. Early motion has also been possible because our reconstructive surgical techniques have improved through the years. The rehabilitative techniques can be more aggressive because the operations performed today can withstand the forces associated with these rehab programs.

—Dean Taylor, MD



AFTER TENURES AT the World Health Organization and Yale University's School of Public Health, internationally renowned HIV/AIDS expert Michael Merson chose to head in Duke's direction, becoming the leader of our new, university-wide Global Health Institute in November. The institute was created this spring to give intensified focus, resources, and coordination to interdisciplinary efforts that address global health issues, with the ultimate goal of improving the health of underserved people in Durham and internationally. We wanted to know why Merson sees his new post down South as an ideal move in an already worldly career.

3 Three questions

Talking globally with Michael H. Merson, MD, director, Duke Global Health Institute

Is global health getting more notice in spheres beyond medicine and public health?

Yes, global health has become a major political issue—it's now on the political agenda of national leaders and heads of donor and UN agencies. Health issues have been on the agenda of the last five G-8 conferences.

There has also been a substantial increase in funding for global health over the past five years. A good example is the largest foundation in the world: the Gates Foundation, which awards $3 billion a year in grants. It's made global health its primary focus.*

There is no doubt that global health is attracting research interest among those working in a wide range of academic fields: economists, social scientists, engineers, and lawyers as well as those in medicine and public health.

Why do you think people are paying more attention to world health and health disparities?

I can think of three reasons. First, there is now recognition that health and health care must be part of any strategy for economic development and political stability. People who have poor health are usually living in poverty, and often they live in societies where there is social and political instability. There's a vicious cycle that's created, and any strategy against it must address health along with poverty alleviation.

Secondly, there's now a worldwide consciousness about the impact of pandemics. We have seen three examples in recent decades: One, the AIDS pandemic, which has been with us 25 years and is now the number-one cause of mortality in the developing world. The SARS pandemic came and went relatively quickly, but it had an enormous economic impact, particularly in Asia. Now there's the threat of avian flu as a pandemic that could have profound impacts in rich and poor countries.

Third is the growing popularity of the idea that no matter where we live, we have a basic human right to access to medications and vaccines. Eradicating health disparities over access to medications is now a critical issue around the world.

What was it about Duke's strategy for the new Global Health Institute that compelled you to lead the effort?

As more focus has been placed on health as an issue that affects development at every level, there has also been a clearer understanding that to work successfully in global health, we need to harness many different disciplines—not only to understand the social and economic determinants of health, but also to develop interventions that really will improve the health of populations. What impressed me about Duke was its very rich and vibrant tradition of interdisciplinary work, and its commitment to drawing on the intellectual assets of the entire university to solve global health problems. I was also attracted by the idea of directing an institute that would undertake educational, research, and service-related activities.

Learn more about Merson on page 52 and about Duke's Global Health Institute at globalhealth.duke.edu.

*In July the Bill & Melinda Gates Foundation awarded Duke two grants totaling $46 million to further HIV/AIDS research, as part of the Foundation's $287-million Collaboration for AIDS Vaccine Discovery. For more information, see page 30.

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 Duke Winter Anesthesia and Critical Care Review	March 4-11, 2007	The Canyons Resort, Park City, UT	20 credits	919-681-6437
INTERNAL MEDICINE 2007 EBM: A Workshop for Teachers and Champions of Evidence-based Medicine	March 20-23, 2007	R. David Thomas Executive Conference Center Durham, NC	35 credits	919-681-3009
RADIOLOGY A Practical Approach to Musculoskeletal MRI	February 17-20, 2007	Disney's Grand Floridian Orlando, FL	20 credits	919-684-7228
23rd Annual Duke Radiology Review	April 15-20, 2007	Sheraton Imperial Hotel Research Triangle Park, NC	49 credits	919-684-7228
PET/CT & Neuroimaging Update	April 28-May 1, 2007	Charleston Place Charleston, SC	17.5 credits	919-684-7228

ONLINE

COURSE	DATE	CREDIT	REGISTRATION
CONTINUING MEDICAL EDUCATION A Case-based Approach to Understanding the AMA Guidelines on Gifts to Physicians, OIG, and New ACCME Standards	Through May 31, 2007	1 credit	cme.mc.duke.edu/wysiwyg/downloads/Duke_Case_Based_Approach_Self_Study_052306.ppt
GASTROENTEROLOGY Integrated Approach to Irritable Bowel Syndrome	Through January 31, 2007	1.25 credits	ja-online.com/dukeibs
INFECTION CONTROL Insertion of Central Venous Catheters	Through January 17, 2007	2.25 credits	cvctraining.medicine.duke.edu
RESEARCH ETHICS "Social Sciences Research in Medical Settings" "Using Databases in Research" "Prisoners Involved as Participants in Research" "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" "The Fundamentals"	All Research Ethics courses are available through December 31, 2006	1.5 credits	For more information or to register, visit: researchethics.duhs.duke.edu

Here's an idea! Get CME credit for reading *DukeMed Magazine*:

Physicians licensed by the North Carolina Medical Board (NCMB) must complete 150 hours of practice-relevant continuing medical education (CME) every three years in order to be relicensed. Up to 90 of the 150 required hours for NCMB relicensure can be "self-claim" credit for physician-initiated activities such as practice-based self study, consultations with colleagues, teaching, M&M conferences, journal clubs, and reading clinically relevant articles in *DukeMed Magazine*. The North Carolina Medical Board provides a form that can be downloaded from its Web site for your use in tracking physician-initiated activities: Visit ncmedboard.org/clients/NCBOM/Public/Physicians/cmerec.htm.

For additional information regarding CME credit for NCMB relicensure, please contact the NCMB at 919-326-1100, 919-326-1109, or 800-253-9653 (toll-free in-state long distance). Physicians licensed by other state boards may also be able to receive "self-claim" CME credit; for information please contact your state medical board.

These activities have been approved for AMA PRA credit.

DukeMed MAGAZINE
VOLUME 6, ISSUE 2, FALL/WINTER 2006

The vaccine hunter

Twenty-five years after the first AIDS diagnosis, the search for a vaccine is more intense than ever. "We've realized that we need to find new ways to harness the immune system, to make a vaccine the likes of which has never been made," says Duke's Barton Haynes, MD.

Haynes now leads a worldwide network of scientists who are training their sights on that very goal. And he believes the unprecedented global cooperation and investment in this "grand experiment" will change the way we approach medical crises of this magnitude. "We are asking," says Haynes, "whether virtual consortia, in which scientists collaborate in a manner that doesn't extinguish or suppress serendipity, could be more effective in coming up with answers to the great pandemics of our age."

Read more on page 30.

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