

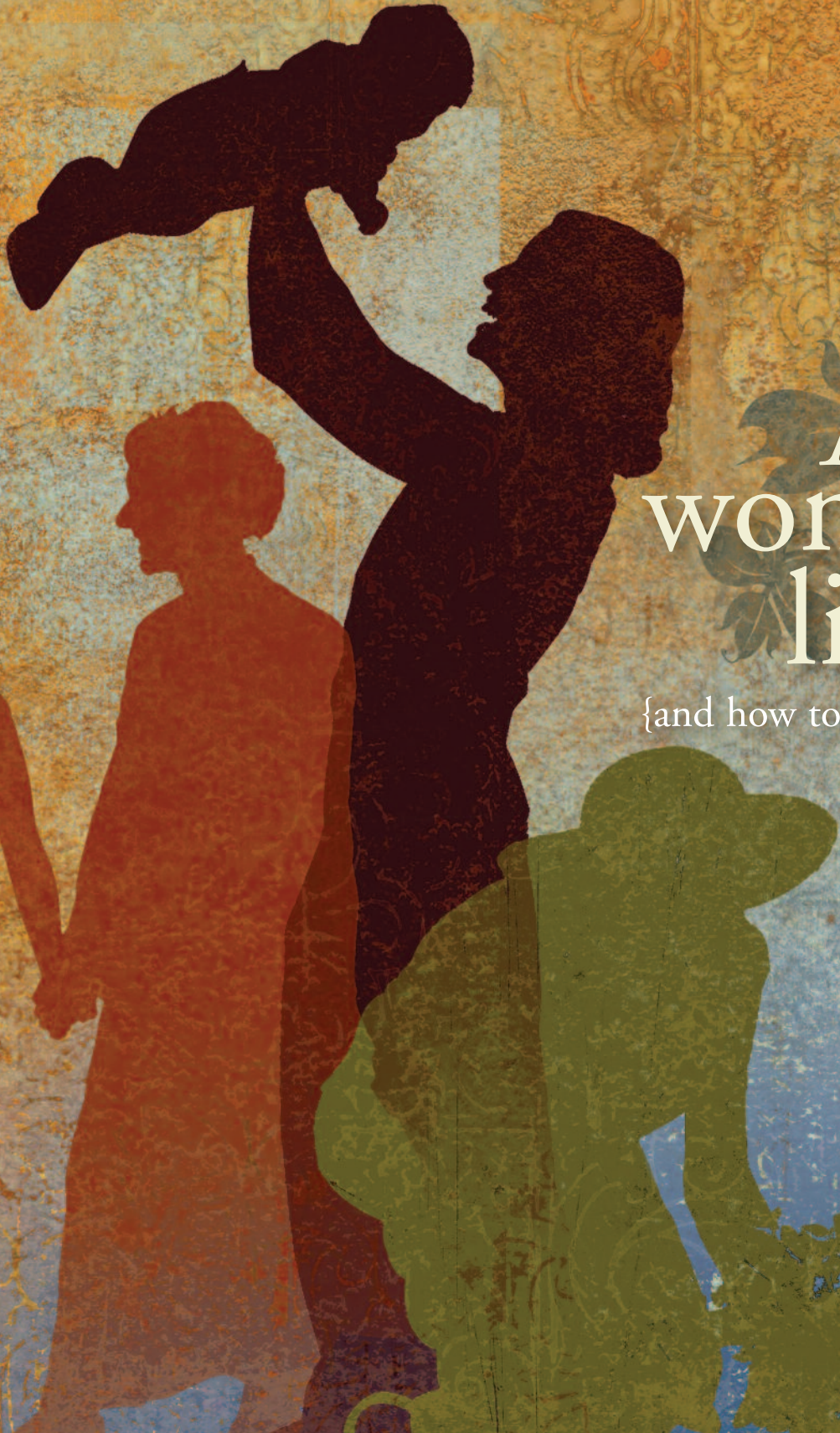
❖ Implantation's pivotal role 20

❖ Hormone replacement therapy 40

❖ Debilitating osteoporosis 50

VanderbiltMedicine

WINTER 2008

The cover features a series of silhouettes against a textured, warm-toned background with floral patterns. At the top, a dark silhouette of a man holds a baby high in the air. Below him, a reddish-brown silhouette of a woman stands to the left, and a reddish-brown silhouette of a child stands to the right. In the foreground, a green silhouette of a person wearing a wide-brimmed hat is shown from the back, looking towards the family. The overall composition suggests a focus on family, health, and the life cycle.

A woman's life

{and how to take care of it}



East meets West

In October 2007, a group affiliated with the Vanderbilt Alumni Association and Vanderbilt Medical Alumni Affairs traveled to China, on an exciting exploration of the Middle Kingdom. The itinerary included all the expected highlights: The Great Wall and Forbidden City, a three-day cruise on the Yangzi River, and Shanghai, China's most European-influenced city.



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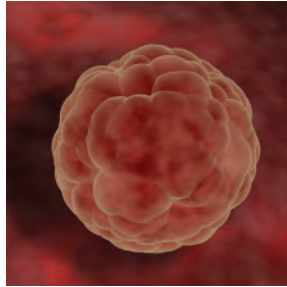
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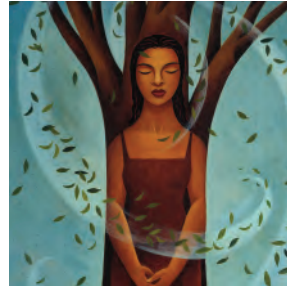
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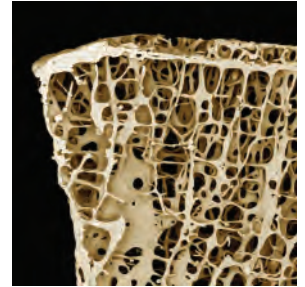
A woman's life is filled with many milestones and a multitude of health risks. *Vanderbilt Medicine* takes a look at some of the obstacles along the way.



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A MIGHTY BOND 12

BY STEVEN G. GABBE, M.D.

Dean, Vanderbilt University School of Medicine

For the better part of my career as a physician,



DEAN DIXON

I have focused my attention on the particular health needs of women. For that reason I'm especially proud that our Department of Obstetrics and Gynecology was ranked 10th in the country by *U.S. News and World Report*. This issue of *Vanderbilt Medicine* surveys the sweep of women's health through the life cycle. Understanding the consequential differences between men's and women's health was perhaps the first step toward personalized medicine. It was not a startling conclusion that men and women are different – physiology being what it is. It is understanding the subtle as well as obvious differences that makes the study of women's health so intriguing. Women are different physiologically, but also metabolically, biochemically and evolutionarily.

Disease among women can present very differently from men. Take heart disease, for example. All of our classic understanding of heart attack is based on its manifestation in men. When surveyed about the threats to their health, women overwhelmingly list breast cancer as the highest threat even though the most deadly cancer for women is lung cancer and the most life threatening disease is cardiovascular.

Obstetricians and gynecologists have generally cared for mom and baby from the moment of conception until birth. New genetic tools, fetal diagnostics and even fetal interventions such as *in utero* surgery to correct spina bifida have dramatically changed all that. Pediatric specialists are now often intimately involved in monitoring and managing mom and baby during pregnancy. So closely tied are the two practices, especially in managing high-risk pregnancies, that we plan to

expand the Monroe Carell Jr. Children's Hospital at Vanderbilt to accommodate a new obstetrics unit focused on at-risk mothers so that neonatal care and pediatric specialists are close by.

As women age, their health concerns turn dramatically around menopause. From the onset of menopause, health risks for cardiovascular disease surge, osteoporosis becomes a significant concern, and cancers of the breast, ovaries and uterus become more prevalent. Menopause and the decline in estrogen production that accompanies it are intimately linked to each of these diseases. These observations led many to conclude that replacing the hormones of youth could forestall the onset of these diseases. But life turned out to be not quite so simple. Hormone replacement therapy (HRT), once considered the lead candidate to reduce heart disease among older women, in fact, elevated the risk of cardiovascular disease for many of the women who took it. And it is clearly implicated in raising the incidence of certain cancers among women.

Yet for all the dashed expectations of HRT, it still holds promise for women and is the subject of continuing examination by scientists and doctors here at Vanderbilt. This and other women's health research has been dramatically stimulated by the NIH Building Interdisciplinary Research Careers in Women's Health (BIRCWH) grant recently renewed for another five years. Vanderbilt is one of only 15 such centers nationally. The next decade will be one of greater understanding, but also greater challenge, in women's health. We are excited to be at the leading edge. **VM**

Medical School names first Master Science Teachers

As a way of rewarding its most outstanding science educators, Vanderbilt University School of Medicine has named seven faculty members to its first group of Master Science Teachers.

They will collaborate with the 13 Master Clinical Teachers to integrate the basic science and clinical components of the new curriculum.

Named as Master Science Teachers are: Neil Osheroff, Ph.D., professor of Biochemistry; Cathy Pettepher, Ph.D., professor of Cancer Biology; Art Dalley, Ph.D., professor of Cell and Developmental Biology; Luc Van Kaer, Ph.D., professor of Microbiology and Immunology; Lillian Nanney, Ph.D., professor of Plastic Surgery; Jim Atkinson, M.D., Ph.D., professor of Pathology; and Jeanette Norden, Ph.D., professor of Cell and Developmental Biology.

The Master Science Teacher program is designed to enhance medical education and protect time for teaching, as well as to improve the teaching skills of VUSM faculty members, said Dean Steven Gabbe, M.D.

"We hope they will serve as role models for other faculty to become better educators. We're trying to broaden our efforts to provide a curriculum of education for our faculty," Gabbe said.

Department chairs submitted nominations for Master Science Teachers. They are compensated for their participation in the program, which will occupy 5 percent to 20 percent of their time. The Dean's office provides the funding, said Bonnie Miller, M.D., associate dean for Undergraduate Medical Education.

"They have so much pressure to be productive on their grants, that teaching, if it doesn't get funded in some specific way, gets put on the back burner. That's just a reality of an academic medical center. We feel that these are excellent teachers, and funding their teaching effort puts it on the same level as their other responsibilities," Miller said. **VM**

—KATHY WHITNEY

News and happenings at Vanderbilt Medical Center

In pursuit of personalized medicine

Vanderbilt University Medical Center has been selected to participate in and coordinate a national network that will pursue the ideal of personalized medicine — health care "tailored" to each individual's genetic makeup.

The network of five sites, collectively awarded \$20 million by the National Institutes of Health, will evaluate how electronic medical record systems can be used for large-scale genetic research.

Principal investigator Dan Roden, M.D., said Vanderbilt was well-positioned to compete for the new grant because of the institution's investments over the last few years in the DNA Databank Resource, an anonymous collection of genetic and clinical information.

"The idea was to create a large collection of DNA samples that are associated with clinical information, and to do that in a way that preserves patient privacy and yet allows investigators to access the very rich information that we have in the electronic medical record," said Roden, assistant vice chancellor for Personalized Medicine.

"It is gratifying that the NIH has recognized our efforts in conceptualizing and building the DNA Databank," said Harry Jacobson, M.D., vice chancellor for Health Affairs. "We expect that this resource will enable researchers to discover genetic links to disease susceptibility and drug response that will ultimately personalize and improve patient care. Our participation in this new consortium will move us toward that goal more quickly."

Sample collection for the DNA Databank resource, which is directed by Jill Pulley, M.B.A., launched in February, and Roden said he expects the resource to hold 50,000 samples by next May.

Each center in the new consortium, organized by the National Human Genome Research Institute (NHGRI) with additional funding from the National Institute of General Medical Sciences, will study the genetic variation underlying a particular human trait using a technique called genome-wide association analysis.

"The NHGRI essentially challenged institutions to come up with proposals that will test how useful our collections of DNA samples and electronic records really are for genome science," Roden said.

Other sites participating in the network are Marshfield Clinic, Mayo Clinic, Northwestern University and the University of Washington. **VM**

—LEIGH MACMILLAN



Dan Roden, M.D.

New curriculum, enhanced facilities greet Class of 2011

The Vanderbilt University School of Medicine Class of 2011 began their medical school journey in August, the first class to benefit from the new integrated curriculum throughout its four years of training and the first to use more than \$10 million in new educational facilities — including the Center for Experiential Learning and Assessment, with its state-of-the-art Standardized Patient Center and Simulation Center, and a new anatomy laboratory on the top floor of the Vanderbilt Institute of Imaging Science.

This year's class is more than prepared to take on the role of pioneers. As Harry Jacobson, M.D., vice chancellor for Health Affairs, pointed out during orientation, they are an exceptional group, which boasts an average MCAT score of 11.5 and a collective 3.8 GPA.

The 104 incoming first-year medical students span 30 states including Tennessee (20), Florida (10), Georgia (4), California (10), New York (5), and nine are citizens of other countries, including Canada, Ethiopia, India, Republic of Korea, Poland, Taiwan and Thailand.

Together they represent 51 different colleges and universities, with 16 having completed their undergraduate work at Vanderbilt and 19 representing Ivy League schools, including seven from Harvard University.

Upon completion of the "Foundations of the Profession" course, first-year students received their white coats in a ceremony on the lawn of the Chapman Quadrangle. **VM**

—KATHY WHITNEY

Pediatric liver transplant program debuts

The Monroe Carell Jr. Children's Hospital at Vanderbilt has launched the region's first pediatric liver transplantation program.

While older children, mostly teenagers, have been receiving liver transplants through the adult liver transplant program at Vanderbilt and similar programs across the region, the new pediatric program is the first to specialize in infants and children.

"Last year we had 600 visits for liver disease in children from newborns up to 18 years old," said Lynette Gillis, M.D., medical director of the Pediatric Hepatology and Liver Transplant Program. "This year we are on target to see 700, so our medical program is large and has seen significant growth."

Burnett "Beau" Kelly Jr., M.D., assistant professor of Hepatobiliary Surgery and Liver Transplantation, serves as surgical director.

The United Network for Organ Sharing (UNOS) matches donors with recipients. Vanderbilt is part of an "administrative region" that includes Tennessee, Kentucky, North and South Carolina and Virginia, but Kelly says livers can be brought in from almost anywhere if they are a good match.

"We can go anywhere in the country, if the quality of the organ is appropriate and matches the needs of the patient," Kelly said. "The need is definitely there, so part of our mission will also be education about organ transplantation."

Brent Polk, M.D., interim chair of Pediatrics, medical director and physician-in-chief of Children's Hospital, said the new program will enhance patient care.

"Adding the transplant surgery will now permit our patients, their families and friends to remain in the same supportive environment as they await and receive their transplants. I am proud to be a small part of this exciting advance in our department and hospital," Polk said.

"This program will enable Middle Tennessee children with liver disease to receive world-class care right here in their backyard," said Ravi Chari, M.D., chief of the Division of Hepatobiliary Surgery and Liver Transplantation.

"For families, it will alleviate the burden of travel. We have two excellent stewards and leaders of the program in Drs. Beau Kelly and Lynette Gillis. Transplantation truly demands 'team medicine' and that demand plays to their, and Children's Hospital's, strengths." **VM**

—CAROLE BARTOO



The pediatric liver transplant program team includes from left, Beau Kelly, M.D., Lynette Gillis, M.D., Nurse Practitioner Carly Bhava and Donna Williams, R.N.



Jonathan Haines, Ph.D.,
in a genetic research lab
in Light Hall.

Cracking the genetics of MS

The genes that contribute to multiple sclerosis (MS) have been defying identification for more than 30 years.

Only a single gene locus has been found to contribute strongly to MS; no other genes — of the more than 100 that have been associated with the disease — have reached consensus.

Now, a multi-center team has provided solid genetic and functional evidence for a gene linked to MS. The Multiple Sclerosis Genetics Group, which includes investigators at Vanderbilt University, reported in *Nature Genetics* that the interleukin 7 receptor (IL7R) alpha chain gene is associated with MS. The finding offers fresh opportunities for investigating the molecular causes of MS and seeking new therapeutic options.

“The genetics of MS has been very difficult to crack,” said Jonathan Haines, Ph.D., director of the Center for Human Genetics Research at Vanderbilt and senior author of the paper. “This is the first MS-associated gene outside of the major histocompatibility complex that has been confirmed in multiple populations. It gives us insight into a new signaling pathway that we can now hopefully exploit to identify targets for treatment.”

MS is an unpredictable, chronic inflammatory disease of the central nervous system. It destroys the myelin sheaths around nerve cells, causing a range of symptoms including visual problems, muscle weakness and disability. MS is thought to result from a complex interplay of genetics and environmental triggers and affects about 350,000 individuals in the United States.

The MS Genetics Group used a powerful technique called “genomic convergence” that integrates multiple sources and types of evidence to implicate candidate genes in complex diseases.

“We took a very systematic approach,” said Margaret Pericak-Vance, Ph.D., director of the Miami Institute for Human Genomics at the University of Miami and a senior member of the MS Genetics Group. “We looked at multiple lines of evidence that would give us the best chances of successfully identifying a gene that was truly involved in MS susceptibility.”

Using the genomic convergence approach, the investigators selected three candidate genes, which they analyzed in a group of 760 Caucasian families that included 1,055 MS patients. They identified a significant association with MS susceptibility for a single variation in one of the three genes — the IL7R alpha chain.

Candidate genes have had a spotty history when tested beyond the initial study.

“This has been the big knock on candidate gene studies in complex disease: they almost always fail to replicate,” Haines said, although this study proved otherwise. **VM**

—LEIGH MACMILLAN

VUMC named to evidence-based medicine initiative

Vanderbilt University Medical Center has been chosen as one of 14 Evidence-based Practice Centers (EPCs) in the United States and Canada, according to the Agency for Healthcare Research and Quality (AHRQ).

For a decade AHRQ has systematically reviewed and reported on the content and quality of the medical literature on specific topics like choice of depression treatments, prostate cancer screening options and surgical outcomes for knee replacement.

The groups that conduct the reviews and summarize the implications are called the Evidence-based Practice Centers.

EPCs evaluate the state of the science of specified topics by performing rigorous reviews and analyses of scientific literature, making options more clear for patients with complex or life-threatening diagnoses who face a bewildering array of information and treatment options, for doctors who must consider new reports of possible harms for treatments that have been mainstays, and for payers who have to weigh the potential benefits and costs of coverage of new drugs, procedures and diagnostic tests.

EPC topics encompass clinical, preventive, behavioral, organizational and financial aspects of health care.

Ancillary analyses, such as claims data analyses or use of advanced models to demonstrate potential outcomes of alternatives, are also performed by EPCs.

The end result is a combination of existing knowledge termed an Evidence Report, used by groups including federal and state agencies, private sector professional societies, health delivery systems, providers and payers.

“This selection says that the AHRQ believes we have top-notch scientists and a strong infrastructure to produce scientifically rigorous reports and materials to help inform care,” said Katherine Hartmann, M.D., Ph.D., director of the EPC. **VM**

—NANCY HUMPHREY

Cancer Center embarks on campaign to raise \$10 million

Vanderbilt-Ingram Cancer Center has launched a \$10 million capital campaign to fund expansion of the Henry-Joyce Cancer Clinic.

Construction has already begun on the project to dramatically expand the clinic and provide a more comfortable, healing environment for patients and their families, in addition to improving research areas.

"We are making headway toward meeting our goal, with \$3.6 million already pledged by donors in early conversations about this campaign," said Orrin Ingram, chair of the Board of Overseers for Vanderbilt-Ingram and co-chair of the expansion project.

"We know many families have experienced the devastation of cancer and we hope this giving campaign will provide them an opportunity to make a difference in the lives of cancer patients and their families."

Built nearly 20 years ago — and a decade since its last significant expansion — the cancer clinic is past due for renovation. There were nearly 52,000 patient visits last fiscal year — an increase of nearly 60 percent since 2002. With America's aging population, demand for cancer care will continue to grow.

Without this extensive renovation the cancer clinic simply cannot accommodate all of the patients who need access to the center, consistently ranked among the best in cancer care by *U.S. News & World Report*.

The construction will double the square footage available for cancer care on the first and second floors of the clinic, and double the number of chemotherapy chairs, which will reduce wait times for patients. The renovation also will provide more space for research, including the ability to offer more clinical trials.

The \$16.5 million - \$20 million renovation project is scheduled for completion in late 2008. **VM**

—DAGNY STUART



Like chocolate-covered strawberries

Coronary artery disease — fatty plaques clogging the heart's supply lines — can produce chest pain or heart attacks, and is responsible for more than half of all cardiovascular disease in the United States.

Vanderbilt University Medical Center investigators have discovered a role for a growth factor receptor in the development of coronary blood vessels. The findings, reported recently in *Circulation Research*, may offer a new therapeutic target for directing coronary artery growth or repair, a possible alternative to bypass surgery.

It has become clear over the last decade that the coronary blood vessels are unique, said Joey Barnett, Ph.D., associate professor of Pharmacology and senior author of the new study.

They do not — as older textbooks suggest — branch from the aorta and grow to feed the embryo's developing heart. Instead, a small "packet of cells" near the embryonic liver migrates to the heart and coats its surface "like chocolate covering a strawberry," Barnett explained. That coating becomes the heart's outer protective layer, the epicardium. Some of the coating cells invade the heart muscle and assemble the coronary vasculature. The vessels then attach to the aorta to complete the coronary circulation.

"The fact that these cells have a unique origin may explain why coronary arteries have certain types of disease pathologies, and might also provide us with new opportunities to fix these arteries," Barnett said.

Barnett and colleagues have been pursuing how growth factors, in particular those in the TGF-beta family, participate in heart development. To examine the role of the "type III" TGF-beta receptor, Leigh Compton, Ph.D., a student in the Medical Scientist Training Program, knocked out the receptor gene in the mouse. Mice missing the type III TGF-beta receptor gene died *in utero*, at embryonic day 14.5, when functional coronary vessels are required for further development.

"It was striking that these mice don't make coronary blood vessels," Barnett said. "Every other blood vessel we examined appeared to be present and normal, but not the coronary vessels."

The findings suggest that the type III TGF-beta receptor plays a unique role in supporting coronary blood vessel growth, Barnett noted.

"And since more than 700,000 people in the United States will have coronary artery disease this year, identifying a molecule that's specifically required for coronary vessel formation is really exciting." **VM**

—LEIGH MACMILLAN

Antidepressants: Are they safe during pregnancy?

BY CAROLE BARTOO



KARIVANTINE/IMAGES.COM

Research led by a physician at the Monroe Carell Jr. Children's Hospital at Vanderbilt shows that the number of women who use antidepressant drugs during pregnancy is rising despite a lack of proof the drugs are safe for their unborn babies.

The study, published recently in the *American Journal of Obstetrics and Gynecology*,

combed 1999-2003 data from the medical records of more than 100,000 pregnant women in the TennCare system, Tennessee's Medicaid Managed Care Program.

William Cooper, M.D., associate professor of Pediatrics at the Children's Hospital and the study's principal investigator, said the records show the use of antidepressant medications increased from 5.7 percent of pregnancies in 1999 to 13.4 percent of pregnancies in 2003.

"We were a little surprised by the increase because many women stop taking medications when they find out they are pregnant," Cooper said. "It highlights the importance of knowing more about these medicines, especially during pregnancy. We just don't know enough to make informed decisions about the use of many drugs for pregnant women."

Exposure to antidepressants during early and late pregnancy has been associated with birth defects of the heart and high blood pressure in the baby's lungs, but the data are limited. The most common type of antidepressants used in this study was selective serotonin reuptake inhibitors, but Cooper found exposure to all types of antidepressants was more frequent in the first trimester than the second or third.

The numbers also showed mothers who were older (over 25), Caucasian, and who had higher education levels were more likely to take antidepressants during pregnancy than other women.

Cooper is quick to say the study doesn't suggest women who suffer from clinical depression should not be treated

during pregnancy; rather, he says, it shows the importance of studying potential side effects for babies more thoroughly.

"It is important to note that untreated depression can also put the baby at risk. This study points to a need for women to work with their health care provider to find the best treatment plan that works for them."

This collaborative study with the Food and Drug Administration may lead to further research nationally. Cooper said TennCare data are a great place to start for a study like this because 50 percent of women giving birth in Tennessee are on TennCare. The large, diverse population is a good testing ground for the FDA's theories about potential problems within the medication prescribing system nationwide.

"It's a large population with a broad variety of life circumstance," Cooper said. "That gives more weight to the findings and indicates that health care providers who care for women – and women who may become pregnant – need to be given clear information about the safety of these medications. We don't have that information to give them now." **VM**

ROSE MARIE ROBERTSON, M.D.



A heart career

WHILE ROSE MARIE ROBERTSON, M.D., was serving as president of the American Heart Association, she made a simple observation – there was a stark contrast between what the organization was attempting to accomplish and what physicians were able to do for their patients.

“We had a tremendous amount of science telling us what to do to help people with heart disease and stroke, but there were enormous barriers to patients getting the actual care they needed,” recalls Robertson, professor of Medicine at Vanderbilt.

“There were enormous disparities in health care and the opportunities for people to have good health care. When I saw the opportunity to do something for people in the broader sense of health care, it felt worthwhile,” she said. “Many decisions about the health care system get made without physician input and there are many places where physicians, whose focus is the good of the public, can have a real impact. We have a knowledge base that allows us to think about problems in a way that only people who take care of patients think.”

As Robertson’s role as president of the AHA was winding down in 2002, another post became open on the national level that would require a leave of absence from Vanderbilt. In 2003 she was named chief science officer at the AHA. It was an opportunity that would allow Robertson

to continue to make a difference in public health policy – something that meshes her interest in both clinical care and patient-oriented research.

Since the start of her career, Robertson has shown a propensity for research. She credits Vanderbilt for helping mold her love for science as well as provide her the opportunity to practice.

“Vanderbilt could not have been a better place to have been a faculty member,” said Robertson, 62. “It’s always been characterized by effective interactions between basic science departments and clinical departments. There was a remarkable lack of hierarchical barriers to collaborations. That is not characteristic of all places.

“From a science career point of view, it is a wonderful atmosphere to grow up in, if you will, and I certainly benefited.”

Best friends and partners

Robertson, who is married to David Robertson, M.D., Elton Yates Professor of Autonomic Disorders and professor of Medicine, Pharmacology and Neurology at Vanderbilt, has had many opportunities to collaborate with her husband on research projects.

“I’ve been very fortunate to have been able to share a career working with

my husband in science,” she said. “You can’t be luckier than to have your closest collaborator be your best friend and your partner in all other things.”

The pair has shared many exciting research milestones from investigating the causes and effects of coronary artery spasm in the Coronary Care Unit to working on an experiment on NASA’s shuttle and SpaceLab. The Robertsons and colleagues founded the Association for Patient-Oriented Research, a group of investigators who focus on how to provide the best support for clinical investigators to do the most critical clinical research in an effort to solve the multitude of questions and problems facing patients.

But perhaps their best collaboration is daughter Rose Marie, 24, a budding fiber artist who works with and creates textiles.

It wasn’t until their only child graduated from college that Robertson was willing to consider a larger role at the AHA because of the extensive travel requirements and longer stints away from home.

She is happy that her schedule allows for frequent visits with her daughter while traveling on AHA business as well as time at home with her husband.

“Thank goodness for video conferencing,” Robertson said. “It cuts down on some of the travel – but not nearly enough! Sometimes we do feel like ships that pass in the night. But it makes you focus more when you are at home. There is no question – travel is the part of this that is the most difficult for us. We’d rather we weren’t in different cities as much as we are, but it always feels great to get back home. I couldn’t do this if David didn’t believe in the value of what I do. The key is to have a wonderful husband.”

Rose Marie Robertson grew up in Detroit. Her mother was a physician and practiced until she was 73 years old. Her father died when she was only 4.

Although she briefly considered English Literature while in college at Manhattanville College in New York, she followed in the footsteps of her mother, a family practitioner, and attended Harvard Medical School, graduating in 1970. She

trained in internal medicine at Massachusetts General Hospital and in cardiology at Johns Hopkins.

Rose Marie and David Robertson met while at Johns Hopkins Hospital and discovered through friends that they were both coming to Vanderbilt to work in 1975. They decided it was more affordable to rent a truck together to move their belongings. Although not dating at the time, that meeting proved to be monumental. They married in 1978, and decided to make Nashville their home.

Spreading the word

Robertson was the first female cardiologist at Vanderbilt and the first Vanderbilt physician ever elected to the post of president of the AHA.

Working for a nonprofit organization with the task of eradicating heart disease and stroke has had a huge impact on her. Although her medical practice concentration was cardiovascular medicine, in time because of her work with the AHA, women's heart health became a point of interest.

Robertson was the first female cardiologist at Vanderbilt and the first Vanderbilt physician ever elected to the post of president of the AHA.

While still a full-time faculty member at Vanderbilt, she started the Women's Heart Institute, which served as a preventive cardiovascular care practice for women.

Robertson said the AHA was instrumental in that development.

"If you were a woman and president of the AHA, people assumed the issues of women and heart disease were your focus, even if it wasn't your specific area of research," she said.

"It hadn't been mine, but I became a de facto spokesperson on cardiovascular disease in women at that time," said Robertson. "It became clear to me, and it was certainly clear to my AHA colleagues, that women really didn't understand how heart disease affected them, nor did their

physicians. There was a great deal of work to be done to educate women, raise awareness among physicians and educate the population at large.

"Certainly to put the words 'women' and 'heart' in the title of an institute makes a statement. It means there must be a reason to have such a program, and it helps women to pay attention to those issues."

And still the work continues – her message today centers around youth and heart disease. There is a misconception that heart disease is an ailment of menopausal women and middle-aged men, she said.

"There is good evidence that women in their 20s have the beginnings of heart disease," she said. "Women need to start early to prevent later problems and that means living a healthy lifestyle. We are making headway on that message and trying to bring it down even to children."

Since the first efforts to raise awareness about women and heart disease, additional programs have popped up to promote women's heart health including Go Red for Women, an awareness cam-

paign to educate women about their risk of heart disease; Start, a new program encouraging employers to create a healthy environment for walking/physical activity and nutrition at work; and Get with the Guidelines, a hospital-based program for patients with coronary heart disease, stroke and heart failure.

"Get with the Guidelines is almost identical to the discharge order sets we have in our very sophisticated electronic health record at Vanderbilt," Robertson said. "It's nice to know that Vanderbilt was way ahead of the curve on that."

Recently she became involved in another national health issue – obesity. As the chief science officer, she has taken the lead in this initiative, helping guide the

AHA in its work on childhood obesity with the William J. Clinton Foundation and California Governor Arnold Schwarzenegger.

Robertson's work has not gone unnoticed. In 1993 she received the Gold Heart Award from the Tennessee AHA affiliate, and in 1999 was honored by the national group with the Award of Meritorious Achievement for rendering an important service to the AHA in the development of its national programs. In 2001 she was given the Partner in Public Health Award by the Centers for Disease Control and Prevention (CDC) in recognition of her leadership in developing partnerships among agencies in the fight against heart disease and stroke and mentoring health care professionals in the area of cardiovascular disease.

Working in the nonprofit arena has offered Robertson not only a window to see the health needs of the communities around her, but a door she has opened to make a difference.

Robertson says that volunteer activity provides people opportunities they might not have had on their own. When she is testifying before a congressional committee and representing a major national organization, people listen.

"Often legislators don't listen enough. But when there is the power of a group representing millions of individuals behind you, they are more likely to pay attention. I would encourage people in general to become engaged in nonprofit organizations. It's a great way to impact your community as well as meet and work with like-minded people who want to make a difference and make the world a better place."

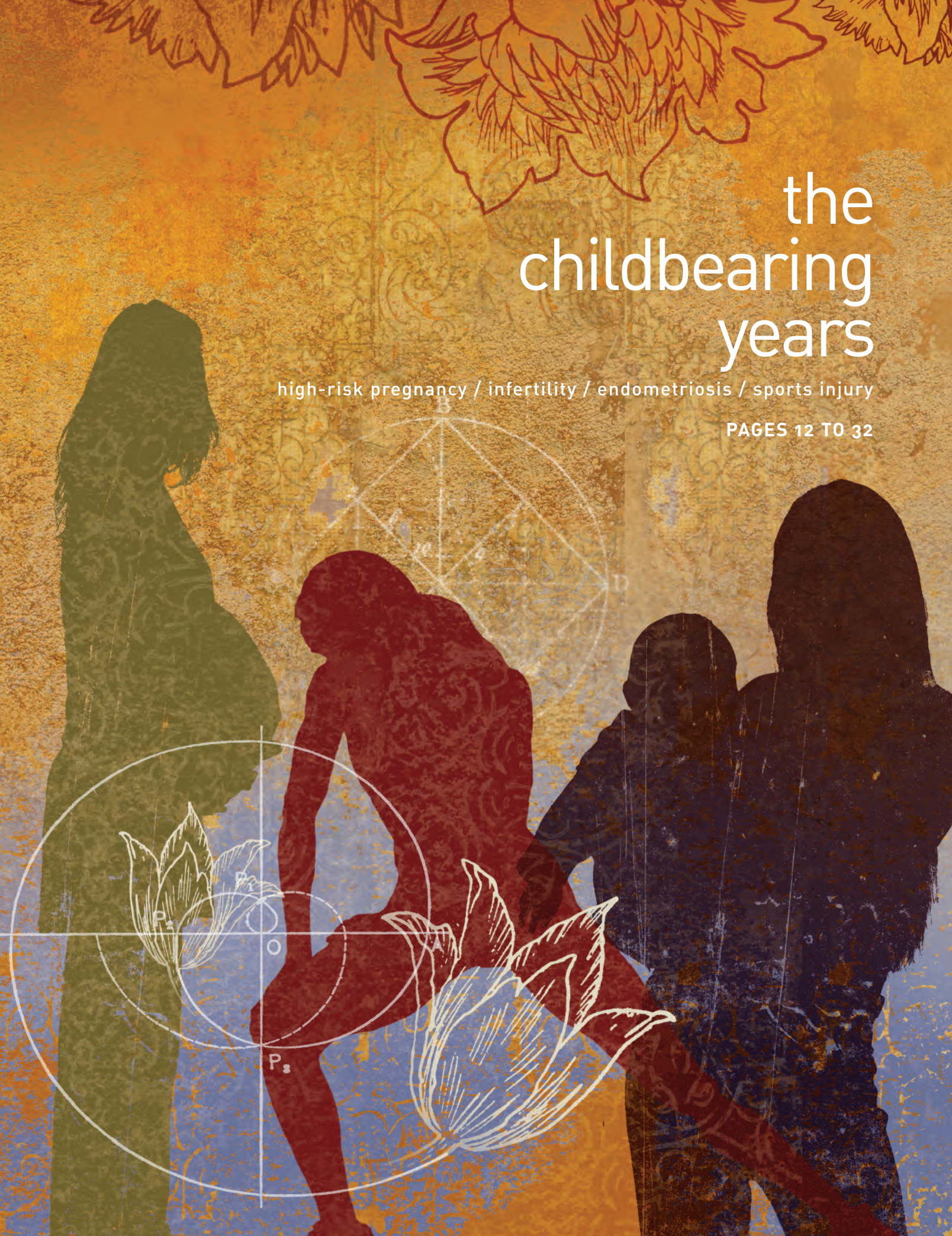
Robertson is grateful that she has had the opportunity to have an impact on health care.

"Appreciate the great lives we get to lead. We can take great satisfaction in the value of what we do. We can wake up every morning knowing we'll get to make a real difference. Not many people get to do that." **VM**

the childbearing years

high-risk pregnancy / infertility / endometriosis / sports injury

PAGES 12 TO 32





Heather Cornell and Tyler



mighty bond

Neonatology and Obstetrics are two medical practices with two very different types of patients, but Judy Aschner, M.D., director of the Division of Neonatology at the Monroe Carell Jr. Children's Hospital at Vanderbilt, has an appropriate analogy. "They are connected by an umbilical cord," she says with a smile.

WRITTEN BY **CAROLE BARTOO**
PHOTOGRAPHY BY **TAMARA REYNOLDS**

Aside from being a compelling visual, it's also a fact:

neither can work effectively in exclusion of the other. And by working closely together at Vanderbilt, those who practice the specialties are offering hope to many Middle Tennessee area families.

The relationship that has developed in just the last three to five years has already been so successful that critically ill, or premature newborns treated at the neonatal intensive care unit (NICU) at the Children's Hospital have higher survival rates and lower complication rates than babies in most other NICUs across the country. The success of Vanderbilt's NICU program is well recognized by many delivery hospitals in the region that depend on the Vanderbilt Neonatal Angel Transport team for a fast and efficient plan to get babies to Vanderbilt.

Heather Cornell found out about that efficiency when she went into labor with her first baby. She had no warning, excellent prenatal care and no previous sign of early labor – but sometimes babies just come early. Her doctors delivered

Heather's first baby, a son named Tyler, at just 27 weeks gestation, or about three months early. She delivered him in Bowling Green, Ky.

"They told me they were calling Vanderbilt before they even began my delivery," Heather said. Tyler weighed a tender 2 pounds, 6 ounces. Heather only got to touch his tiny foot for a moment before an Angel Transport team carried him on a 50-minute journey to Vanderbilt so he could receive the care he needed.

"My husband and his mother said goodbye to me while I was just out of surgical recovery, then drove to Nashville," Heather said. "It was very scary... terrifying."

Many families who deliver critically ill or very premature babies away from a Level 3 NICU may be divided almost immediately.

"If a baby is born elsewhere, the baby is whisked off, mom stays to get her treatment at the birthing hospital while dad tries to broker between two places and

two loved ones (the mother and the baby), so collaborations are really important," said Nancy Chescheir, M.D., the Betty and Lonnie S. Burnett Professor and Chair of the Department of Obstetrics and Gynecology.

"I had (Tyler) on a Monday and stayed in the hospital until Wednesday," Heather said. "They wanted me to stay longer but I wanted to get to Vanderbilt." She and her mother left the birth-hospital without even stopping at home first, "because (Vanderbilt) was where I was supposed to be; where I needed to be. I needed to know he was OK, not just for him – for me."

The Cornell family was reunited and was able to rest in the family sleep rooms adjacent to the critical care unit. Heather, who developed an infection in her incision site, said the next six-and-a-half weeks were among the toughest she could imagine.

"I never thought my husband and I could go through something like that, but we did," she said. "We still call on the Children's Hospital for advice and reassurance, even now that Tyler is a rambunctious 10-month-old."

Fixing the problem

The difficulties of separating families at birth and transporting infants are vexing problems for those who work in both Obstetrics and Neonatology. High-risk Obstetrics at Vanderbilt University Medical Center and the Neonatal and Pediatric practices at the Children's Hospital now officially combine efforts in the Division for Advanced Maternal-Fetal Care and a corresponding Center at Children's Hospital. Together, Vanderbilt experts are working to address many social, political and medical issues tied up in the question of how to improve the care of infants and mothers. It is an important topic for the state of Tennessee as well, which ranks just seven marks from the bottom of the barrel (43rd) in infant mortality.

It's a shameful designation that Vanderbilt wants to help change. The Center, funded in part by a \$2 million,



Heather and Derrik Cornell with Tyler

TAMARA REYNOLDS



Tyler Cornell, 10 months

six-year pledge from the Junior League of Nashville (JLN) is growing quickly. A recently announced plan for an expansion to the Children's Hospital may give a new face and facility to women and children's health in the region. A \$5.4 million planning budget has been approved for the proposed \$203 million, eight-floor Women's and Children's expansion, which could be open by 2012.

Leaders in the areas of maternal-fetal care and neonatology at Vanderbilt say Tennessee languishes at 43rd in the nation for infant mortality at least in part because of an outdated view of how to best improve the outcomes of pregnancy: that current view focuses almost exclusively on the babies after they are born. They argue that to make a significant improvement in birth outcomes in Tennessee, intervention must begin with their mothers.

"The infant mortality rate for babies born two months or more before their due date (about 32 weeks or earlier) is 75 times higher than for full-term babies," said Aschner, Neonatology's director. "We

cannot effectively reduce infant mortality if we don't partner with mothers and their obstetricians to change the rates of pre-term and low birth weight births."

Aschner, Chescheir and Maureen Malee, M.D., Ph.D., director of the Division of Maternal-Fetal Medicine, have all practiced medicine in other states where infant mortality rates are much lower. They wonder: "Why aren't more women in Tennessee receiving better prenatal education and care?" and "Why aren't more families partnering with specialists to develop a game plan to help unborn babies with congenital defects in the early stages of pregnancy, rather than right before birth?"

The questions are many, and the problem is both expansive and expensive. The good news is it's finally beginning to top the list of concerns for state officials.

In March of 2006, the Tennessee Comptroller's office came out with a report that laid out the startling facts:

- ■ More than 30 percent of children who die in Tennessee are infants who are born prematurely.

- ■ Birth defects are the leading cause of death among white infants, while low birth weight is the leading cause among black infants.

- ■ The rate of death among black infants is 2.7 times higher than that of white infants.

In 2005, according to 2000-2002 data from the Tennessee Department of Health, Tennessee's infant mortality rate of 8.8 per 1,000 live births was ranked the third highest in the nation. The Tennessee infant mortality rate during this period was 31 percent higher than the national average. The 2004 mortality rate for Tennessee black infants was 17.4 per 1,000 live births, compared with a mortality of 6.4 per 1,000 live births for white infants.

Mothers are at risk, too

"We have a terrible problem here in Tennessee," said Chescheir. "Infant mortality is often a direct result of the treatment or care of women in this state. We do not do well right now with women's health.

When pregnant women suffer complications it's bad for everybody – baby and mom too – and it's terrible for the state.”

“We have high rates of diabetes, obesity, high blood pressure, smoking, substance abuse, poor nutrition,” chimes in Malee. “Mothers are at risk as well as babies. The maternal mortality rate in the U.S. is higher than that of many other countries in the world, maybe because mothers don't get diagnosed. One serious societal problem is that while babies and children in Tennessee are well covered by TennCare, Tennessee's Medicaid managed care program, their mothers are not.

Anyone over age 18 is subject to recent cutbacks in the adult coverage of TennCare; so many mothers simply don't have good care available to them before they become pregnant.”

The single greatest contributor to infant mortality is not the care of the infant, but the health and lifestyle of the mother before the baby is born. Focusing on saving babies once they are out of the womb is getting more expensive every year.

“Finding better, more effective treatments for prematurity was my goal for many years,” said William Walsh, M.D., chief of Nurseries at Children's Hospital,

who bends every ear he can find about his 'million-dollar babies.' “But I now realize that it would be better to focus research and energy on prevention of prematurity. The focus on prematurity has to be twofold. We know the money spent on one preemie could potentially prevent 10 preterm births. We are working hard to identify the factors responsible for prematurity. The best outcome is not a surviving preemie but a healthy term baby.”

Inborn vs. Outborn

One of the major issues the state is studying is the “inborn” versus “outborn”

The MOMS trial

Some of the most devastating news a pregnant woman can receive about her unborn child is that it has a birth defect. The most frequently occurring permanently disabling birth defect in the United States is spina bifida, which occurs in about 1.5 to 2 out of every 1,000 live births when the spinal column fails to completely close during the first month of pregnancy.

Vanderbilt University Medical Center is one of three hospitals in the country participating in the randomized, controlled MOMS trial (Management of Myelomeningocele Study) sponsored by the National Institutes of Health. Doctors with experience in fetal surgery from Vanderbilt, The Children's Hospital of Philadelphia, and the University of California at San Francisco are enrolling 200 women in the study. Half of the babies will receive fetal surgery and half the traditional surgery a few days after birth. They are randomly chosen for

one type of surgery or the other and then followed for two and a half years or longer to determine whether infants operated on *in utero* suffer the same disabilities as those operated on as newborns and whether the results outweigh the risks to both mother and child.

The trial began in 2003 and enrollment is about 60 percent complete, says Ed Yang, M.D., Ph.D., assistant professor of Pediatric Surgery and medical director of the Center for Advanced Maternal-Fetal Care at Vanderbilt. It's taking longer to enroll women than the study investigators would like, but the outcome will be a clear message on the safety and efficacy of fetal surgical repair, Yang said.

“We think it will take another two to three years to recruit patients, then we'll have to follow the patients for another two and a half years at a minimum, so this trial could be going on for another five years. It takes incredible institutional commitment to stay with this, and we have

that here. We're looking at 2012 before we're done and during that time we could be developing newer approaches, advancing the way we do this operation and subselecting different populations within the population we're studying, but we're just kind of stuck. It's incredibly frustrating because we can't advance in our care beyond this operation.”

Yang said enrollment is slow because of two reasons: the incidence of spina bifida has been declining because of the use of folic acid by pregnant women, and because women have either not heard about the trial or they think it has been completed.

“We're constantly trying to communicate with the obstetrics community who sees these patients that the trial is still ongoing,” he said. “It's going to tell us a lot about how the operation works, the risks, benefits, long-term issues of patients and the mom, how the child's bladder works after fetal surgery versus standard care, etc.”

Since the 1930s the first step in treatment of babies

with spina bifida has been surgically closing the opening in their back a few days after birth. The surgery prevents further damage to and infection of the nerve tissues but doesn't restore function to the already damaged nerves. A shunt is usually placed within the ventricles to drain excess fluid and relieve pressure in the brain.

Research has shown that spinal function in babies with spina bifida seems to worsen throughout pregnancy. It is believed that there is ongoing damage to the open portion of the spinal cord, possibly from contact with amniotic fluid. Because of this research, in 1994, doctors began trying out various methods for closing spina bifida defects in the womb. The fetal surgical procedure is done at 19 to 25 weeks of pregnancy.

Vanderbilt's fetal surgery team includes several specialties, including ethicists who meet with families during the evaluation process.

—NANCY HUMPHREY

population in NICUs. “Inborn” babies are those whose mothers deliver at the same hospital where high level neonatal care is available, so that the prenatal and post-delivery care is as seamless as possible. “Outborn” babies are transported after delivery at another hospital to a hospital with a high level neonatal care, often necessitating separation of mother and baby and subjecting the infant to an ambulance or helicopter transport when the baby is in a tenuous medical condition.

Aschner says a critical factor in deciding where to deliver babies at high risk for surgical complications should be whether there are pediatric surgeons and pediatric anesthesiologists and an appropriate level NICU at the delivery hospital. But 42 percent of very low birth weight babies, and 45 percent of extremely low birth weight babies cared for at the Children’s Hospital are still outborn.

“And that percentage is increasing, which is very concerning, because babies who are brought in from elsewhere have significantly more complications and are less likely to survive than those who are inborn,” Aschner said.

Aschner is quick to point out that compared to other children’s hospitals that care for the sickest newborn patients, the complication and survival rates for all babies treated at the Monroe Carell Jr. Children’s Hospital NICU, regardless of where they were born, are among the best in the nation. That speaks well of the Children’s Hospital NICU and of the birth hospitals in the area, but there is a significant advantage for babies who are inborn and treated in one place, with the appropriate level of care and expertise. Aschner says it is important to explore ways the playing field can be leveled for all babies.

“We know, for example, in the extremely premature infants, bleeds in the brain are three times more common for outborn babies than for those who are inborn. Rates of surgery for potentially fatal gastrointestinal blockages and perforations are four times higher for outborn babies,” said Aschner.

Surgical repairs and post-surgery care are a huge contributor to health care costs, but even for premature or small babies who just need to be supported in a NICU (nurses call them “feeders and growers” because they are so small and underdeveloped), the cost of care runs quickly into the tens of thousands of dollars. In the U.S. the average cost for caring for a preterm infant in a NICU is \$33,200.

For the Thurmans, another Bowling Green, Ky., family, it will be more. They are parents of premature twin baby girls, Grace Ann and Addyson Marie. The Thurmans, who have good health

\$33,200

THE AVERAGE COST
OF CARING FOR
A PRETERM
INFANT IN A NICU

DANA JOHNSON



Addyson Marie Thurman weighed 3 pounds, 6 ounces, when she was delivered at 32 weeks. Close observation at Vanderbilt gave her a few extra weeks in the womb.

insurance, know they will likely never know the full cost of caring for their babies. Patty Thurman’s doctors knew early on that she would need care at the Vanderbilt Maternal-Fetal Care Center.

“My doctor in Bowling Green sent me down here to the Maternal-Fetal Care Center when I was 25 weeks along. He had noticed Grace Ann wasn’t growing like she should,” Patty Thurman said.

Because Grace Ann had an underdeveloped placenta of unknown cause, there was no way to avoid a preterm delivery. The goal was simply to last as long as possible without compromising the health of either baby too much for the benefit of the other.

“I ended up making it to 32 weeks and one day before we had to deliver them to save Grace Ann,” she said,

Left to right: Nancy Chescheir, M.D., Maureen Malee, M.D., Ph.D., and Judy Aschner, M.D., are part of a leadership team working to blend obstetrics and pediatrics.



The single greatest contributor to infant mortality is not the care of the infant, but the health and lifestyle of the mother before the baby is born.

adding that her babies gained at least a couple of weeks in the womb from careful observation at Vanderbilt. While Grace Ann was still very small at birth, just 1 pound 8 ounces, Addyson Marie might have benefited the most from the extra time in the womb, weighing a much more robust 3 pounds 6 ounces.

“Addyson has been doing great,” Thurman said. “She only had to use the ventilator for a little while but she is on room air now. Now we’re starting to talk about how we will handle it when Addyson gets to go home before Grace Ann.”

While the Thurman family knows their daughters’ care will likely be very costly, they may not realize how much

money was actually saved by very careful prenatal planning and Patty’s dutiful bedrest. According to the U.S. Department of Health and Human Services, an increase of one-half pound in birth weight saves an estimated \$12,000 to \$16,000 per baby in first-year medical expenses.

Getting the word out

Aschner says a simple and logical solution is to spread the word throughout Middle Tennessee that women with high risk pregnancies like those carrying multiple babies ... or women carrying babies with known birth defects should consider delivering at a hospital like Vanderbilt with high level maternal-fetal and pediatric care.

“We are the only facility in the state with a comprehensive fetal surgery program, including a number of prenatal interventions that can make dramatic differences in survival,” Aschner said. “We are the only center in the region that has pediatric surgical sub-specialists trained in the repair of all major birth defects.”

Doctors would like for all babies to be success stories, like Mia Bowers. Mia’s mother, Amanda, found out that her baby had a major birth defect, spina bifida, at just 18 weeks of gestation.

“I was told I would lose the baby or that I should consider an abortion,” recalls Bowers.

Her doctors at another Nashville hospital ultimately recommended she come to the maternal-fetal care program at Vanderbilt, because of the program’s experience in treating spina bifida.

The Center for Advanced Maternal-Fetal Care is only one of three such centers in the U.S. currently involved in the only National Institutes of Health-funded trial on fetal surgery. The study, called the MOMs (Management of Myelomeningocele) trial, is examining the use of fetal surgery to close the spinal columns of babies with spina bifida – long before the babies are born.

While it turned out Bowers’ baby was not a candidate for the MOMs trial, her baby developed under the watchful eye of a whole team of pediatric specialists, including a neurosurgeon, neurologists, and a heart expert called in to watch a hole in the lower chambers of Mia’s developing heart.

Bowers surprised herself by delivering her daughter full-term. After the Caesarean section, Mia briefly met her mother then was brought to the NICU for the careful observation of the sac-like protrusion over the opening in her spine. Surgery to close her spinal column was performed successfully the next day.

“At first I thought I would not like delivering at Vanderbilt, but the nurses and everyone have been great. Now I wouldn’t have done it anywhere else,” Amanda said. “I am glad I can walk over and see her. It is a long walk (she smiled) but it is comforting to know if anything was happening, she is just down that hall.”

There may still be some work to be done to prove to families that Vanderbilt’s labor and delivery program is among the best. Because it is a smaller program than others in town, the message is not widespread.

“Here at Vanderbilt we have an extraordinary amount of specialized care available,” Malee said. “Each of these mothers has a diagnosis that can be

1/2 LB

AN INCREASE OF ONE-HALF POUND IN BIRTH WEIGHT SAVES AN ESTIMATED \$12,000 TO \$16,000 PER BABY IN FIRST-YEAR MEDICAL EXPENSES.

worked up, not just by our specialists in maternal-fetal care, but also at the Diabetes Center and the Heart Center. Mothers with Lupus can see a rheumatologist, those with seizure disorders can get care from a neurologist. Simultaneously, pediatric care can be planned for the baby. We can even offer intervention before the baby is born, if needed with our growing fetal medicine program.”

Tennessee may be getting bad press year-after-year for its infant mortality rate,

but Aschner, herself a mother of four, believes that can change if all hospitals adopt a similar plan to “triage” high risk mothers, early in pregnancy, to birthing centers with the appropriate level of maternal-fetal and pediatric care.

On the neonatal-side, Aschner is pursuing a grant that would help to set up a nine-point treatment plan for all very low and extremely low birth weight babies across the state, so that centers with perhaps fewer sub-specialists on hand can

improve survival rates and outcomes.

Malee and Chescheir say the next challenge will be to convince politicians and women alike that taking care of babies begins with offering high-level health care to all women of childbearing age.

“Half of all births in Tennessee are unplanned,” Malee said. “If we want to help babies be healthier, we have to pull together as a community around the health of women.” **VM**

The holistic approach of the nurse midwife

Across the United States and at Vanderbilt University Medical Center, more pregnant women are opting for certified nurse midwife-assisted births, a consumer-driven trend that is expected to grow. Currently about 10 percent of all vaginal births in the country involve a nurse midwife. Industry sources project that by 2010, nearly 20 percent of deliveries will be nurse-midwife assisted.

Vanderbilt University Hospital has had a successful partnership with the Vanderbilt University School of Nursing integrating nurse midwifery into the hospital’s clinical practice, and positioning nurse midwives in key roles to train with residents during the delivery process. The result is that in fiscal year 2006/2007, more than 700 of the 3,000 deliveries at Vanderbilt were with certified nurse midwives.

“We think it’s very important that our patients have the

option of choosing the kinds of relationship with their provider,” said Nancy Chescheir, M.D., chair of the Department of Obstetrics and Gynecology. “A vast majority of women have perfectly normal, healthy pregnancies and deliveries, and midwives have a very special, holistic approach.”

Tonia Moore-Davis, M.S.N., C.N.M., clinical practice manager for VUSN’s Nurse-Midwifery Faculty Practice, emphasizes that nurse midwifery of today is evidence-based as well as a popular model of care in other countries such as the United Kingdom.

According to the American College of Nurse-Midwives, 85 percent of all births are considered normal and do not require medical intervention. Midwife-assisted deliveries are a low medical intervention option that focuses on physical, emotional and social needs of the pregnant woman and her family. Moore-Davis and her colleagues are exploring additional options to enhance labor and delivery, such as cutting edge pain management options like hydrotherapy and nitrous oxide.

“The point is that it’s not simply your home-grown nurse midwife who is attending,” said Moore-Davis. “It is academic medicine. A lot of programs are incorporating nurse midwives into their faculty and using their expertise to train residents.”

At Vanderbilt, there’s no need to look further than the fourth floor of Vanderbilt Hospital to see nurse midwives and residents working together. Deborah Wage, C.N.M., assistant professor, moved from her clinical practice affiliated with VUSN to head the Division of Midwifery and Advanced Practice for the Vanderbilt University School of Medicine in 2006. She and colleague Angela Wilson-Liveryman, C.N.M., assistant professor, are helping integrate the midwifery model of care into an academic school of medicine. This approach has proven successful at many of the top schools of medicine, and Vanderbilt’s program is well under way.

As a result of this integrated model, experienced nurse midwives can help provide a new perspective that will allow the students to develop

strong clinical skills for the provision of obstetrical care and understand the family-centered approach to delivery.

“In cases of high-risk patients, they help provide clinical care in a co-management arena where midwives team up with perinatologists and maternal-fetal medicine experts, but the nurse midwife is providing the collaboration,” said Wage.

Anecdotally, Wage knows of many residents who have gone on and purposefully chosen practice settings where certified nurse midwives are their colleagues. She believes each resident will leave the Vanderbilt program having seen the “other way” of doing things.

“We are not here to turn residents into nurse midwives,” said Wage. “We are here to respect both approaches and work together for the patient.”

Due in part to the number of patients requesting nurse midwifery services, the School of Nursing practice has expanded to Nashville General Hospital as well.

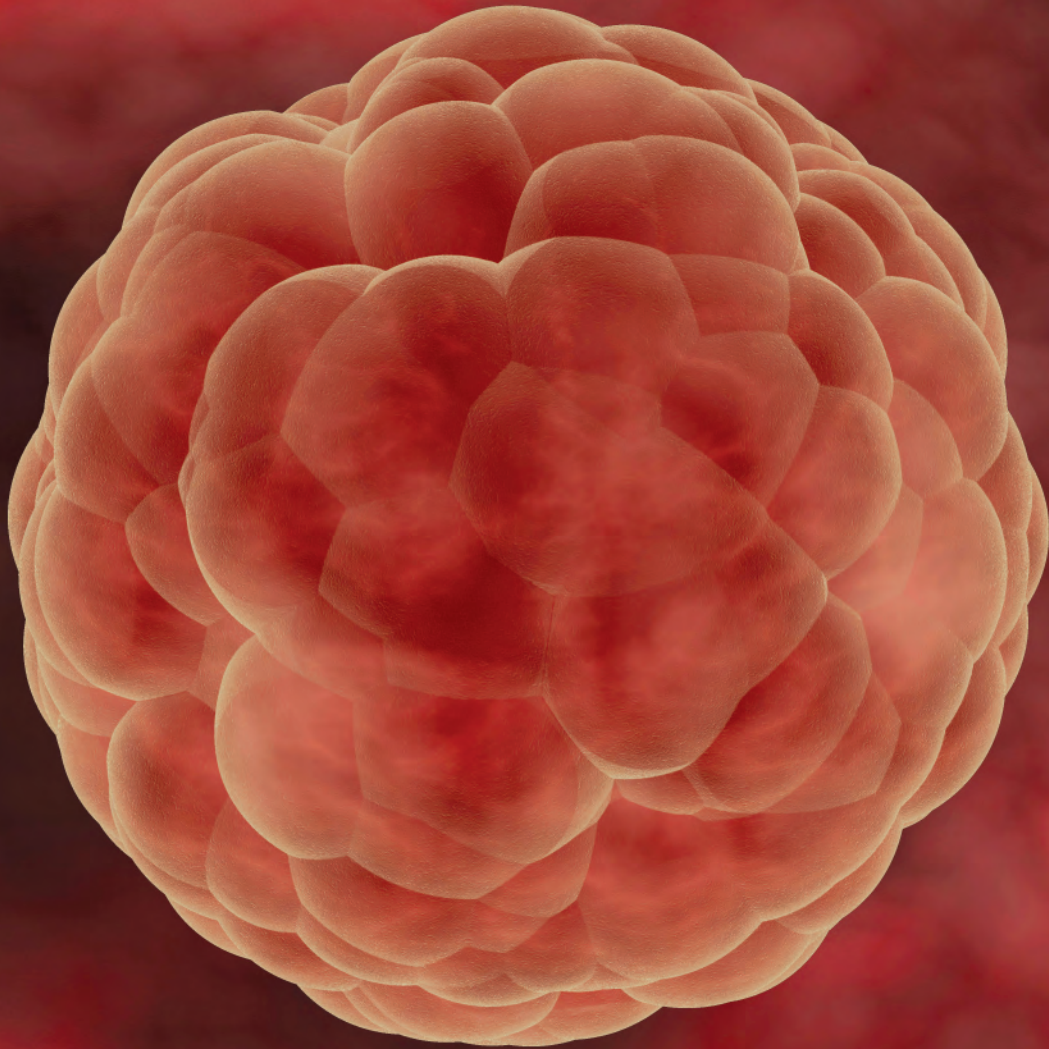
— KATHY RIVERS

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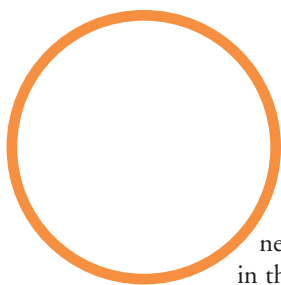
PREGNANCY



implantation's pivotal role



WRITTEN BY **MELISSA MARINO**
ILLUSTRATION BY **ISTOCKPHOTO**



One of the most important moments in the establishment of a new life goes by largely unnoticed.

About a week before the first obvious sign of pregnancy – the missed period – a tiny ball of cells that has grown from a fertilized egg grabs hold of the mother’s uterine lining where it nestles in for a nine-month residence. This moment of implantation sets the stage for the remainder of pregnancy, with the slightest disruption threatening the embryo’s future.

The factors that guide this pivotal process remain shrouded in mystery due to the difficulty of studying this hidden and fleeting event. Advancing the knowledge of implantation and the molecules and pathways that guide it is a critical step toward improving birth control methods and understanding and treating infertility.

Researchers in the Division of Reproductive and Developmental Biology at Vanderbilt University Medical Center, led by S. K. Dey, Ph.D., are using animal models – primarily genetically engineered mice – to identify and characterize the molecules that guide implantation.

INFERTILITY

With around 4 million babies born in the United States each year, conceiving a child can seem deceptively easy. This apparent fecundity obscures the fact that approximately 10 percent of people of reproductive age – or 6.1 million people in the United States – are infertile. The causes of infertility are varied, but about 40 percent involve a female factor.

In vitro fertilization-embryo transfer (IVF-ET) has aided many couples – but it is far from perfect. IVF-ET only has a 30 percent pregnancy success rate, even though the IVF process boasts a 60 percent to 80 percent fertilization rate.

“Many of these failures are likely due to implantation failure,” Dey says. “The uterus has to be receptive and the embryo has to be implantation competent...both have to be synchronized.”

Even in apparently fertile women, about three-fourths of all embryos fail to implant properly, leading to pregnancy loss before a woman even suspects she might be pregnant.

An incomplete understanding of the basic mechanisms of early pregnancy events has limited progress in treating infertility.

“Uterine biology and embryo-uterine interactions are so unique and involve so many cells that we don’t really understand the process of implantation in depth,” says Dey, the Dorothy Overall Wells Professor of Pediatrics, professor of Cell & Developmental Biology and Pharmacology, and director of the division.

Hormones from the ovary – estrogen and progesterone – signal to the normally inhospitable uterus to prepare it to receive the developing embryo (at this point, called a blastocyst). If, at the end of its journey down the fallopian tubes, the blastocyst finds the lining of the uterus properly prepared, it attaches, secretes enzymes and undergoes cellular changes to help it burrow into the uterine wall where it continues its growth.

This “window of implantation” – when the uterus is receptive and the blastocyst is competent – is brief. And timing is critical.

“Implantation is the gateway to a successful pregnancy. If you tinker with the window of implantation – even by a few hours – it creates an adverse ripple effect throughout pregnancy...and pregnancy outcome is very poor,” says Dey, the first Vanderbilt investigator to hold two simultaneous MERIT (Method to Extend Research in Time) awards from the NIH.

Dey and colleagues have demonstrated the outcome of this deferred implantation “ripple effect,” which can manifest itself in mice by reduction in size of the litter. For example, a normal litter size is eight to nine pups. If implantation is deferred, the mother may give birth to only two to four pups, and they are usually smaller.



THIS “WINDOW OF IMPLANTATION” – WHEN THE UTERUS IS RECEPTIVE AND THE BLASTOCYST IS COMPETENT – IS BRIEF. AND TIMING IS CRITICAL.

In 2003, Dey showed that the window of uterine receptivity depended on a very tight range of estrogen levels. By giving ovariectomized pregnant mice daily doses of progesterone, the researchers kept the developing embryos in a state of “delayed implantation,” where the embryos lay dormant for several days, awaiting the proper signals for implantation. They then tested varying levels of estrogen, finding that a single injection of just 3 nanograms of estrogen kept the uterus receptive for up to four days. Higher doses shrunk the receptive window considerably, sometimes blocking implantation.

The study showed that high levels of estrogen alter the expression of implantation-related genes in the uterus, abolishing uterine receptivity to the embryo. Using genetically engineered mice, Dey is hopeful that he will be able to find ways to extend the receptive phase.

Although it is not clear if delayed implantation occurs in humans, it is clear that estrogen also plays a key role in implantation in humans. Estrogen levels can reach very high levels following some fertility treatments and from exposure to environmental chemicals that mimic

estrogen (xenoestrogens) and dietary plant estrogens (phytoestrogens), posing a possible threat to implantation or alteration of the window of implantation.

Dey’s group found out the hard way that phytoestrogens influence the implantation process when his group moved to Vanderbilt in 2002. Many of the studies he had been conducting for nearly 30 years at his former post at the University of Kansas Medical Center were not working in his new location.

“This was a nightmare coming to Vanderbilt,” he recalls. Even though they were using the same strain of mice from the same source, they couldn’t replicate several experiments that they had performed in Kansas – a major worry in continuing their research.

“Many factors could be responsible for these observed differences between the two sites – animal bedding, water, viral load in the environment and mouse chow. Among many factors, we chose to focus on mouse chow. The mouse chow used here has higher plant estrogen levels (than that used in Kansas),” says Dey. “So, the staff veterinarian arranged for two types of diet – with low phytoestrogen and high phytoestrogen – and we found out the difference.”

They found that the diet with high levels of phytoestrogens altered uterine responses to estrogen and the expression of genes regulated by estrogen. The diet also shifted the implantation window ahead approximately four hours.

Seeing the implications of their study on the larger research community, Dey and his colleague Haibin Wang, Ph.D., assistant professor in his division, who led the study, presented their findings to the National Institute of Environmental

Health Sciences (NIEHS) in an effort to convince feed companies to standardize their diets. But perhaps most significantly, the findings could be clinically important for women who consume diets containing significant sources of phytoestrogens, such as soybeans.

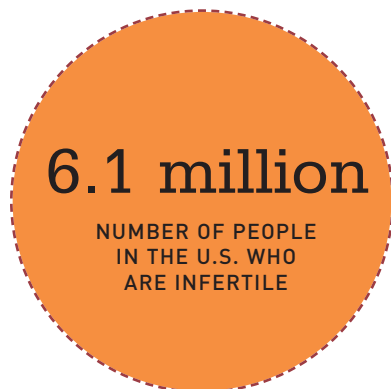
Another potential problem is exposure to chemicals in the environment that can act as estrogen mimics. Dey’s colleague, Sanjoy K. Das, Ph.D., has investigated whether some of these environmental estrogens – the pesticides kepone, methoxychlor and DDT – might still be harmful even though they exist only at very low levels in the environment.

“There is a controversy surrounding these compounds...because they have not been used in this country since the 1970s. But they are very stable compounds. They are not quickly degraded and still persist in the environment in the soil and in the water. Humans can be exposed to them through consumption of plant products and fish,” says Das, associate professor of Pediatrics and Cancer Biology.

The three compounds are known to have estrogen-like (estrogenic) effects – they increase uterine weight and uterine cell proliferation – but only at very high doses.

“We thought that even at lower concentrations, they might be potentially estrogenic, and we have provided molecular evidence in this regard, particularly with kepone.”

Das and colleagues found that low levels of kepone – but not of the other two compounds – have potent estrogenic effects due to the amplifying actions of a natural protein in the body called Bip. By increasing the expression of Bip in the mouse uterus, Das found that low doses of kepone increased cellular proliferation,



Sanjoy Das, Ph.D., left, and S.K. Dey, Ph.D.



uterine weight and the expression of genes that control uterine growth – similar to the effect of high doses of natural estrogen. Such changes may make the uterus nonreceptive to embryo implantation and might even lead to uterine cancer.

Because Bip expression is induced by stress, Das proposes that stress might increase a person's susceptibility to the estrogenic effects of these compounds. At least, this happens in mice.

"This strongly suggests that environmental factors can lead to the induction of this protein (Bip), which may amplify the harmfulness of these estrogenic compounds even at low doses."

Dey's group is also using mouse models to probe the actions of progesterone – the ovarian hormone known as the "hormone of pregnancy." Progesterone plays a major role in implantation and pregnancy maintenance, but how it supports these events is not clearly understood.

Studies led by a graduate student in Dey's lab, Susanne Tranguch, have shown that FKBP52, a co-chaperone molecule that optimizes progesterone receptor signaling, plays a role in female reproduction: mice lacking the *Fkbp52* gene have complete implantation failure. Recently, the researchers reported that progesterone supplementation restores embryo implantation in *Fkbp52* knockout mice on one genetic background, but not another, and that to maintain the pregnancy past implantation requires higher levels of daily progesterone, suggesting that progesterone signaling is a function of genetic makeup and pregnancy stage. The findings may have clinical relevance for women who are infertile and/or have endometriosis due to progesterone resistance.

CANNABINOIDS

Although the classic "female" hormones estrogen and progesterone may be the most obvious areas of implantation research, another class of molecules called cannabinoids also plays a key role.

Marijuana is perhaps the most "famous" source of cannabinoids, but cannabinoid-like chemicals (endocannabinoids) are also found naturally in our bodies where they act as neurotransmitters in the brain and are responsible for the cognitive effects of marijuana.

But they came to Dey's attention when he saw a study showing abnormal breast development in some male Vietnam veterans who were chronic marijuana smokers – which, in a male, indicates excessive estrogen effect.

This sparked Dey's interest in the compound's possible role in the female reproductive cycle and fertility. Over the past 10 years, Dey has become an international leader in the field and has launched the only program of its kind in the country to study endogenous cannabinoid (endocannabinoid) signaling during early pregnancy.

Dey and colleagues presented the first evidence for the presence of cannabinoid receptors in the mouse blastocyst, which they found has 25-times more cannabinoid receptors than the brain. One particular type of endocannabinoid, called anandamide, is produced in the uterus and activates these receptors.

While levels of both anandamide and the receptors are high in nonreceptive uterus and dormant blastocysts, levels drop drastically in receptive uterus and activated blastocysts – showing that cannabinoid signaling must be optimally balanced to synchronize pre-implantation development of the embryo and preparation of the uterine lining.

"Endocannabinoid signaling is important for several aspects of female reproduction – embryogenesis, embryo transport through the oviduct, and embryo implantation," says Dey.

He and his colleagues have shown that when endocannabinoid signaling is dysregulated, the embryo gets stuck in the oviduct. "So it could be a model for ectopic pregnancy," Dey says.



DEY HAS BECOME AN INTERNATIONAL LEADER IN THE FIELD AND HAS LAUNCHED THE ONLY PROGRAM OF ITS KIND IN THE COUNTRY TO STUDY ENDOGENOUS CANNABINOID (ENDOCANNABINOID) SIGNALING DURING EARLY PREGNANCY.

Studies by other investigators suggest a similarly important role for endocannabinoid signaling in human pregnancy, showing that elevated anandamide levels in early pregnancy were associated with an increased rate of miscarriage. Dey is currently working with colleagues at the University of Edinburgh in Scotland on the role of endocannabinoids in human ectopic pregnancy.

“There was anecdotal evidence previously,” says Dey. “But now there is hard scientific evidence that human pregnancy is affected by this signaling.”

COMMON THREAD

Pregnancy can be a pain, literally and figuratively. And much of Dey’s implantation research has focused on compounds best known for their roles in pain and inflammation – prostaglandins and the enzymes responsible for their synthesis, the cyclooxygenases (COX-1 and COX-2).

Dey has focused mainly on COX-2, which is required for synthesis of prostaglandins responsible for the pain of menstrual cramps and the contractions that signify labor. But prostaglandins also play roles in both ovulation and implantation.

Dey and colleagues have shown that ovulation is impaired in COX-2 knockout mice – mice in which the gene encoding COX-2 has been removed. And the few eggs that are fertilized can’t implant in the uterine wall. A normal embryo transplanted into the knockout mouse also fails to implant, suggesting that this process is specifically affected.

COX-2 and consequently prostaglandins influence vascular permeability and new blood vessel growth, which helps prepare the uterus for homing of

the embryo in the womb. A defect in this may be the source of the implantation failure.

“One of the features of implantation is increased vascular permeability at the site of implantation,” Dey says. “You need regulated vascular permeability, so there must be a regulated amount of prostaglandin produced from COX-2. If there is too much COX-2 activity, making too much prostaglandin that would not be conducive to implantation.”

Most recently, Dey’s group has been investigating how COX-2 levels are regulated.

“We have shown that COX-2 is absolutely required for implantation,” he said. “But we didn’t know how COX-2 is regulated in the uterus at the site of implantation.”

In recent years, tiny bits of non-coding nucleic acids, called microRNAs, have come to the fore as important regulators of gene expression, so Dey’s group set out to search for microRNAs that regulate expression of COX-2.

Recently, Dey’s team found that more than two dozen microRNAs show differential expression in the receptive uterus during implantation. Two of these microRNAs were expressed at the same sites as COX-2, and their expression was inversely correlated to COX-2 protein levels, suggesting that the molecules might be important regulators of COX-2.

“Their main function seems to be to dampen COX-2 protein levels,” Dey explained.

The action of these microRNAs might help keep COX-2 and prostaglandin expression at levels amenable to implantation. However, the

tight regulation of COX-2 activity in the receptive uterus goes awry in cancer. Dey’s group also found a similar inverse relationship between COX-2 and microRNA expression in uterine and colon cancer cell lines.

“We see the same molecules [expressed] at the time of implantation and during cancer,” said Dey. “In implantation, they are highly regulated. But in cancer, they are dysregulated.”

“I call this ‘life and death connected by a common thread,’” Dey says. If further studies demonstrate that microRNAs can be manipulated to facilitate or inhibit implantation — or halt cancer — the molecules might represent promising leads for fertility regulation and uterine cancer therapies. Recently Takiko Daikoku, Ph.D., research assistant professor in his group, has undertaken a major study looking at the roles of microRNAs in uterine cancer using genetically altered mouse models.

Although Dey and colleagues have made many seminal findings about the basic mechanisms of implantation with implications for infertility, contraception, uterine and ovarian cancer, ectopic pregnancy and endometriosis, he fears that progress may stall due to increasing budget constraints.

“Shrinking NIH funding and increasing research costs are putting a damper on these programs – programs that are very, very important for women’s health,” he says. “So many opportunities, so many tools, but we just don’t have the resources. This is truly the best time in research and the worst time in research.” **VM**

GENETIC DIAGNOSIS GOES IN UTERO

Children today seem to do things at younger ages: they read, ride bikes, and learn to use computers sooner than did their forebears. They're also being diagnosed with genetic disorders earlier than ever – *in utero*, in fact.

"Genetics has traditionally been a pediatrics subspecialty, because it was devoted to identifying genetic syndromes in children and making sure those children got special care," says Katharine Wenstrom, M.D., professor of Obstetrics and Gynecology. "Now that we know the etiology of many genetic diseases, diagnosis for a wide variety of problems – not just the traditional things – has moved into the prenatal period."

Wenstrom directs the Reproductive Genetics Program in the Division of Maternal-Fetal Medicine. A major goal of the program is to identify fetuses with genetic problems in order to offer prenatal treatments, when available, and improved pregnancy care.

"There are many birth defects that can benefit from prenatal treatment," she says, "and in some cases simply planning the location of the delivery and having certain specialists available can really improve outcome for babies with birth defects and other problems.

"I think in the community prenatal diagnosis is perceived as a search and destroy mission – that we're looking for abnormal pregnancies and the only option is termination. That's not true."

Bladder outlet obstruction, for example, is a rare but usually lethal birth defect. The fetal urine that exits from the bladder is the amniotic fluid that the baby must "breathe" in and out during lung development. Without it, lung development fails. Now, when prenatal ultrasound reveals bladder outlet obstruction, additional tests are performed to determine whether the kidneys are functional. If they are, Wenstrom and colleagues can insert a fetal bladder shunt to divert the urine out of the bladder and into the amniotic cavity, restoring the amniotic fluid volume and thus supporting lung development, as well as protecting the still developing kidneys. A variety of prenatal therapies are available for other kinds of fetal abnormalities.

The Reproductive Genetics Program also offers screening programs for low-risk patients as well as prenatal diagnosis services to patients who are suspected of having a problem.

Wenstrom brings a unique perspective to the program.

She is one of fewer than 50 physicians in the country who are board certified in both Maternal-Fetal Medicine (high risk pregnancy) and in Clinical Genetics. The program also draws on the skills of Martha Dudek, M.S., CGC, a genetic counselor with expertise in prenatal diagnosis. Together, the team interprets screening tests for patients and offers counsel on next steps.

Fetal screening tests of various sorts have been around for decades, Wenstrom notes, but there are now many more general screening tests for low-risk patients and also many specific tests for certain genetic syndromes. Ultrasound technology also has improved dramatically, she points out.

"We're identifying fetal defects prenatally much more often than we used to, and we're able to put all the problems together and make a specific fetal diagnosis much more accurately than we were able to do in the past," she says.

For women whose fetuses have abnormalities, the Center for Advanced Maternal-Fetal Care offers "one stop" care for both the pregnant mother and her baby.

John Pietsch, M.D., professor of Pediatric Surgery, Bill Walsh, M.D., professor of Pediatrics, and Wenstrom are the co-directors of the center

at the Monroe Carell Jr. Children's Hospital at Vanderbilt. The multidisciplinary group includes specialists in Maternal-Fetal Medicine, Neonatology, Pediatric Cardiology and a variety of pediatric surgical specialties including Neurosurgery, General Surgery, Urology and Plastic Surgery. The Center also includes geneticists, social workers and ethicists.

"The patient is evaluated by all the specialists who will impact on her child's care and development, all in a single visit," Wenstrom says. "Then we sit down as a group and discuss optimal management, so the patient gets the benefit of all of us talking to each other to come up with the best plan.

"That is really unusual in my experience."

Wenstrom adds that having an ethicist in the group is particularly important.

"Some of our cases are so unusual that there's no precedent to guide management, and it's not clear what the most ethical and humane course of action is. We decide as a group what we can offer, and what we should offer." **VM**

— LEIGH MACMILLAN



THE COMPLEXITY OF

endometriosis

There's nothing unassuming about endometriosis. As brazen and opportunistic as a cancer, it causes internal scars, cysts and adhesions, which in severe cases can extensively ravage the reproductive tract and surrounding anatomy, often to the accompaniment of unspeakable pain. The disease is a major cause of infertility. It's estimated that \$1 billion is spent on treatment of endometriosis annually in the U.S.

"This is a disease that can affect relationships, marriage, education, work," said Kaylon Bruner-Tran, Ph.D., assistant professor of Obstetrics and Gynecology.

Bruner-Tran's research is focused on cell-to-cell communication within the female reproductive tract. She earned her doctorate at Vanderbilt in 1995 under the mentorship of Kevin Osteen, Ph.D., then returned to join him as a faculty member in 1999.

Endometriosis is a lavish, complex disease that's been hard to pin down.

"For a scientist, it's fascinating the way so many systems and influences seem to be involved with the development of this disease, but that can also become distracting," said Osteen, professor of Obstetrics and Gynecology, professor of Pathology, and director of Vanderbilt's Division of Women's Reproductive Health and Research Center, which houses the flagship academic research program of the Endometriosis Association, an international advocacy group.

With each completed menstrual cycle, the lining of the uterus, called the endometrium, builds up in preparation for pregnancy and then breaks down to be shed in menstruation. A great majority of women have retrograde menstruation, which permits some of the shed tissue to disperse through the pelvic cavity.

In endometriosis, wayward endometrial tissue implants outside the uterus, on the ovaries, fallopian tubes, the outer uterus and its supporting ligaments, the pelvic wall, intestines, bladder and points beyond. The implants build up and shed in rhythm with menstruation, the bleeding causes irritation and thus scarring, cysts, and the fusing or adhesion of normally separate tissues, including adhesions that block the reproductive tract. The pain of endometriosis may extend beyond the menstrual phase, and may include sharp pain during intercourse. Though primarily a disease of the reproductive years, it also can occur in adolescence before menstruation, and it's by no means rare in menopausal women.

WRITTEN BY **PAUL GOVERN**
PHOTOGRAPHY BY **GARY ISAACS/IMAGES.COM**



Endometriosis is the second most common cause of hysterectomy (fibroids are first). While the prevalence of endometriosis among infertile women is put at 40 percent, it's commonly thought that somewhere around 10 percent of all women of childbearing age have the disease to one degree or another.

"We've had students working in our own lab who literally sit and rock from the pain," Osteen said.

"In harsh cases, on a scale from 1 to 10, the pain is 15," said Esther Eisenberg, M.D., professor of Obstetrics and Gynecology and the third member of Vanderbilt's endometriosis team.

Osteen has led laboratory studies that have been highly influential for today's emerging understanding of endometriosis. He is currently a primary investigator for three studies funded by the National Institutes of Health, including two

Research Project Grants (R01) and an Interdisciplinary Research Consortium grant (U54): one study examines progesterone failure in the endometrium of patients with endometriosis; another examines the relationship between endometriosis and the failure of a protective anti-inflammatory protein called CD55; a third study examines whether environmental toxins play a role in endometriosis.

Bruner-Tran is the primary investigator for an NIH-funded study aimed at developing a new model of experimental endometriosis using genetically immunocompromised mice. These mice will allow closer examination of the role of the immune system in the pathophysiology of endometriosis.

The four grants are interactive, with Osteen and Bruner-Tran being co-investigators on each other's grants.

"Translational research can only be successful when basic scientists have clinical partners like Esther. It is essential that physicians and scientists talk to one another," Osteen said.

Endometriosis is a disease that wants not only to be felt, but to be ultimately seen as well. Definitive diagnosis entails visualization, the physician peering through an endoscope as the patient lies anesthetized.

The average time from onset to a diagnosis is currently about seven years. Those years may or may not be pain ridden. Some of the possible sites for implantation of the disease are fully wired for pain, others much less so, and in any given case there's no reason to expect severity of pain to correlate with severity of disease. In fact, it's possible to have considerable damage while remaining pain free.

It would be madness for doctors to order endoscopy for every patient who

reports menstrual pain. On the other hand, the pain of undiagnosed endometriosis has been linked to cases of suicide in younger women, Osteen said. Bruner-Tran said that even though there's no cure, some patients voice tremendous relief upon hearing their diagnosis, because their anguish at last is given a physical explanation.

"It's really a hard disease to study, because you can't get to it early on," Eisenberg said.

There are a number of treatments that can hold the disease and its symptoms at bay, ranging from narcotics to birth control pills for suppression of periods in women not seeking pregnancy to laparoscopic surgery for clearing away implants and diseased tissue.

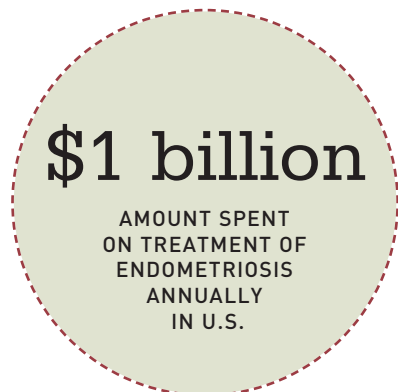
Endometriosis is studied not in humans but in the lab. By the time a patient receives a diagnosis, no one is about to ask her to delay use of a known effective treatment to participate in a clinical trial.

For Osteen and Bruner-Tran, the cause of endometriosis remains elusive, but less so than a decade ago. The known and suspected factors still range from hormonal to immunological to genetic to environmental and epigenetic. The disease continues to invite inquiry of a range and complexity as rich and extended as any in today's medicine. As findings from the lab have mounted, the character and causes of endometriosis have begun to attract greater interest from pharmaceutical companies, and morale among researchers is noticeably higher than it was a decade ago, Osteen said.

Osteen and Bruner-Tran's work is attracting international interest.

"Until Kevin and Kaylon's work came along, no one had really taken the trouble to look closely at the endometrial tissue inside the uterus of patients with the disease; people had instead fixed their attention on implanted tissue outside the uterus," Eisenberg said.

Because endometriosis is primarily a disease of the reproductive years, thinking about the disease traditionally focused on



the role of estrogen, the primary female sex hormone. There was less attention to progesterone, the hormone which, among other things, appears to moderate the immune response in the uterus, such as to allow pregnancy to occur.

“In our lab, we some time ago found reduced sensitivity to ovarian progesterone in the endometrium of women with endometriosis. It sent us on a chase to understand how the disruption of progesterone action might lead to the disease,” Osteen said.

Osteen has more recently linked failure of progesterone to an increased sensitivity to pro-inflammatory signaling compounds, called cytokines; this increased sensitivity may promote earlier than normal degradation of endometrial tissue in menstruation, and may have a role in the development of the disease.

Osteen has also shown an association between endometriosis, progesterone failure, and reduced expression of an anti-inflammatory protein regulated by progesterone, called CD55.

Osteen and Bruner-Tran said half of their current effort in the lab is concerned with understanding what role the environmental toxicant dioxin may have in endometriosis. In particular, they wonder if exposure to dioxin serves to disrupt the equilibrium between the protective capacity of progesterone and the inflammatory action of cytokines.

“Disrupted equilibrium of progesterone and cytokines seems to be a cardinal aspect of the disease,” Osteen said.

In mice, developmental dioxin exposure creates a disequilibrium similar to that of endometriosis. Bruner-Tran has shown that exposure in pregnant mice sets up disequilibrium in adult offspring, and that the echo of this so-called epigenetic effect lasts up to four generations. Bruner-Tran’s refinement of mice as a disease model for endometriosis will be increasingly helpful in the next chapter of research.

“A number of studies have suggested a relationship between dioxin exposure and the development of endometriosis;

Colored scanning electron micrograph of collagen fibers (green) underlying the surface of an endometriotic ovarian cyst. The fibers are immersed in stroma cells (purple), which support the functional areas of an organ. Endometriosis occurs when fragments of the uterine lining become displaced, attaching to other sites in the body. Here the fragment is attached to an ovary.

our studies are really beginning to sort out the tissue-specific mechanisms of dioxin action,” Bruner-Tran said.

“The next step will be to determine what we can do about it,” Osteen said. “Dioxin is a ubiquitous contaminant that we all carry in our bodies. Are there dietary modifications that we can make to better protect ourselves and our children? Our research suggests that the answer is ‘yes.’”

Osteen and Bruner-Tran still face a welter of interesting questions. Is the immunological dimension of endometriosis a cause or a result of the disease? How might inflammation promote endometriosis, and what is the association with other inflammatory processes in the pelvic theater, such as that leading to irritable bowel? How does progesterone inhibit inflammation? What’s the significance of the apparent association, in both humans and lab mice, between endometriosis and increased exposure to certain environmental toxins? What underlies the association of ovarian cancer and endometriosis in the ovary? In what sense is endometriosis an inherited condition? By way of strengthening anti-inflammatory mechanisms, how effective could nutrition be in inhibiting endometriosis? Could more powerful, synthetic versions of progesterone stop endometriosis?

“The broad scope of these questions explains why people once typically gave up on finding a cure,” Osteen said.

“This is a disease that probably has multiple triggers. We can’t limit our thinking to one system. I consider our lab a functional biology lab.



PROFESSOR PIETRO M. MOTTA & GIUSEPPE FAMILIARI / PHOTO RESEARCHERS, INC

“The core mechanisms of the disease and the potential therapeutic targets are beginning to be revealed. Our lab has taken a lead in helping pharmaceutical companies identify potential therapies. I foresee new treatments becoming available in the next five to 10 years that will make this chronic condition more manageable for patients.”

Meanwhile, Eisenberg has adopted a new treatment in her clinical practice that’s not yet well known. For patients with intractable pelvic pain, especially those who’ve already had a hysterectomy or hormone therapy, she’ll often use a combination of fish oil and progesterone or progestin. She explains that fish oil is an antioxidant that may affect the immune response.

“It seems to work for our patients. They feel better. I’ve had patients who come in on high levels of narcotics whom we’re able to help,” she said.

Back in the lab, Osteen and Bruner-Tran have taken note of Eisenberg’s success with fish oil and have begun studying the mechanisms of its action. In particular, they are interested in the ability of fish oil to dampen the impact of dioxin exposure.

“We’ve worked together on this disease for more than 10 years,” Osteen said. “We make a good team.” **VM**

EASY ON THE KNEES



Jen Risper, No. 2, Lady Commodores

FEMALE ATHLETES TODAY MAY PLAY AS HARD AS THEIR MALE COUNTERPARTS, BUT THEY SCORE MORE IN ONE UNFORTUNATE WAY: INJURIES TO A MAJOR STABILIZING LIGAMENT IN THE KNEE.

WRITTEN BY ELIZABETH OLDER
PHOTOGRAPH BY DEAN DIXON

Female basketball players suffer injuries to the anterior cruciate ligament (ACL) twice as often as males in the sport. And in soccer, the injury disparity is even greater; females are four times more likely than males to experience an ACL injury. Volleyball players also are at increased risk.

"It happens in young women," explains Kurt P. Spindler, M.D., professor and vice chairman of the Department of Orthopaedics and Rehabilitation. "It has nothing to do with wear-and-tear and nothing to do with aging."

Females 15 to 25 are at the highest risk; the majority of ACL injuries happen in this group. While researchers have identified ways to help these active young females guard against this ligament injury, the underlying explanation of why women are so much more susceptible is still unclear. Some researchers suggest the injury disparity may be due to differences in conditioning, muscle strength and control, while others point to a possible influence related to

gender, including lower-body alignment and the effect of estrogen on the ligaments.

Jen Risper from Moreno Valley, Calif., knows what it takes to battle back from an ACL injury. The 20-year-old standout defensive Lady Commodores basketball player has done it twice and still is out there competing on the court.

"I've torn my ACL on both legs," explains Risper, a junior Human and Organizational Development major in Peabody College. "The first time was before my senior year of high school. My knee just went out. I landed funny."

But she recuperated and was able to return to playing her final year, and the team went on to win a championship title.

Her second injury, to the right knee, happened on her second day on the Vanderbilt campus. Another player ran into her knee during a pick-up game of basketball, and she faced her second ACL surgical reconstruction in less than two years.

"I was pretty determined to come back and play the same year," she says, which she did after an intense rehabilitation effort.

An all-around sports enthusiast who grew up keeping up with two brothers, Risper likes to join in whatever friendly competition comes her way. She has played basketball since fourth grade, but says she didn't know about the higher risk of ACL injury for young women until she experienced it herself. Now she can tick off the theories espoused by experts to explain why young women have far more ACL injuries than young men.

She thinks girls could benefit from learning playing techniques that might help reduce the likelihood of having an ACL injury, but she believes the training has to start early to be most effective.

"It's really, really hard to re-teach your body how to jump and how to land," she said, explaining that moves become automatic in older players.

"Kids don't know how serious sports are going to be," she says. And learning about body mechanics and balance and

WHILE RESEARCHERS HAVE IDENTIFIED WAYS TO HELP THESE ACTIVE YOUNG FEMALES GUARD AGAINST THIS LIGAMENT INJURY, THE UNDERLYING EXPLANATION OF WHY WOMEN ARE SO MUCH MORE SUSCEPTIBLE IS STILL **UNCLEAR**.

form should be beneficial beyond competitive games, Risper adds.

“Maybe it’s something they could use otherwise in their lives,” she suggests, perhaps to protect themselves from injury in everyday situations, such as slipping and falling.

“They just need to know how to control their bodies,” says Risper.

Besides the physical challenge of getting back into playing shape, Risper acknowledges that she also was affected mentally by her injury experience.

“Coming in as a freshman, you expect a lot from yourself and you want to do a lot,” says Risper. “A way to connect with your teammates is through the basketball court, and that part was taken out of the equation.”

She now sees the second injury, in particular, as a challenge that offered a learning opportunity.

“I think that it can affect you in all areas, but it really is up to you to get the most out of it,” she observes.

While Risper says she can understand why some players walk away from competitive sports after getting injured, she

decided to get back in the game and considers herself better for the experience.

“It helped my character and who I am, mentally and spiritually,” she says.

Arthritis ahead? An ACL injury can have far-reaching effects, since many of the patients who have a good repair outcome will nevertheless go on to develop osteoarthritis at an early age. Even though young women are more susceptible, patients of all ages who participate in certain sports – particularly basketball, football, skiing and soccer – are prone to ACL injuries.

“Most people who tear their ACL are active. They did it playing sports,” said Spindler, director of the Vanderbilt Sports Medicine Center and the Orthopaedic Patient Care Center, and Vanderbilt’s head team physician for NCAA Division I varsity athletes. The ACL, one of four main knee ligaments, connects the shinbone to the thighbone. Running diagonally in the middle of the knee, the ACL keeps the tibia from sliding out in front of the femur and stabilizes the joint during rotation.

To get these patients back into action, ACL reconstruction is done about 90 percent of the time, Spindler says. This entails replacing the injured ligament with a substitute graft taken either from the patient or from a cadaver.

“It’s a very good short-term outcome,” says Spindler, and the patients usually are able to return to playing sports. Less than 10 percent of the patients have instability or graft failure after reconstruction. However, for reasons that still are unclear, some 50 percent to 60 percent of these patients will develop osteoarthritis very early – often about 10

years after the injury at age 30 or so, Spindler explains.

“That affects your lifestyle, your exercise program, your kids,” he says.

Researchers are working to figure out what factors affect this outcome with the hope of learning how to better treat ACL injuries, says Spindler, who is heading up a study funded by a \$1.2 million

National Institutes of Health grant that is gathering data on this problematic outcome. Seven academic institutions and 18 physicians are involved. In addition, Spindler is leading a separate research investigation that will evaluate the outcome for patients who need a second ACL surgery.

While these research efforts are targeting ACL injuries, what scientists learn from them is expected to have broader benefits.

“Most of the gurus think this is the best model for degenerative arthritis in everyone,” says Spindler.

In his basic science research, Spindler is investigating the role of tissue engineering and growth factor in ligament healing. Animal studies have shown that placing a collagen-platelet-rich plasma hydrogel in a ligament wound site aids in healing and recovery. Spindler says another three to five years of research should clarify what promise this treatment holds for humans.

Other than ACL injuries, men and women tend to experience musculoskeletal wear-and-tear and injury in much the same way, says Spindler. And he advises that those young female athletes can decrease their chances of an ACL injury by, ironically, learning to play more like a boy. Women, it seems, land from jumps, turn and pivot, and use their thigh muscles differently from men when playing sports.

“There are some strategies that have some scientific basis to prevent these injuries,” says Spindler. With appropriate training methods, females can learn to bend their knees and use their hamstring muscles more to diminish the chance of an ACL injury, he says.

“The good news is that this is correctable,” he says. **VM**

15 to 25

AGE WOMEN
ARE AT HIGHEST
RISK FOR
ACL INJURIES



the middle years

heart health / uterine fibroids / hormone therapy

PAGES 34 TO 42

Fig. 1.

Knowing when to

ACT

MANY WOMEN IGNORE SYMPTOMS OF NO. 1 KILLER

Although Leanne Busby has been a nurse for 35 years, she ignored the numbness in her arms, shortness of breath and nausea that she often experienced on her late night drives from Cumberland University, where she was the dean of the School of Nursing. She let the symptoms continue for a year, silently wondering from time to time if she might be having a heart attack.

WRITTEN BY **KATHY WHITNEY**
PHOTOGRAPHY BY **DEAN DIXON**

**Leanne Busby at Vanderbilt's
Dayani Center**





thought I had carpal tunnel syndrome, so I didn't say anything about it to anyone," she recalled.

She was 60 years old and without a family history of heart disease. However, she was a smoker and worked long days, which left little time for exercise. A visit to her nurse practitioner set in motion a series of events that ultimately saved her life. When she noticed that Busby's blood pressure was elevated, she sent her to her primary care physician in Lebanon. He examined Busby and asked if anything else was bothering her.

"I told him my arms go numb from time to time," she said. "I told him I had never had chest pain."

He sent her to a cardiologist, who performed an arteriogram to visualize her coronary arteries. It indicated some blockage, but he wasn't overly concerned. He sent her to Vanderbilt.

"I thought I needed a stent (a non-invasive procedure). In the holding area, the interventional cardiologist said I needed open heart surgery and I could not go home until I had it."

Busby had an 88 percent blockage of the left main coronary artery, known, ironically, as the widow maker because complete obstruction of the artery can result in a fatal heart attack and it's most often associated with men.

"I knew enough about that to get frightened," Busby said.

Despite the "widow maker" moniker, some studies indicate that middle-aged women fare worse than their male peers after a heart attack. An Emory study reported that women younger than age 50 were nearly three times more likely to die than men of the same age regardless of their medical history, the severity of their condition, when they were admitted to hospital, and the hospital treatment they were given.

Fortunately, Busby's blockage was detected before she had a heart attack, and she underwent double bypass surgery at Vanderbilt. A year and a half later, Busby, a lecturer at Vanderbilt's School of Nursing, is on a mission to educate women about heart disease and to let them know that when it strikes, it may not feel the way they think it would.

Both men and women think of the "Hollywood heart attack" – when a person is knocked to his knees in excruciating pain. But heart attacks in both genders are very often subtle – pain or discomfort you could put up with, or even no real "pain" at all. Since that's more often the case in older individuals, and since women usually have heart attacks on average at an older age than men, these more subtle symptoms are more often seen in women.

"There are a couple of reasons I want women to know my story," Busby said. "Open heart surgery was a traumatic experience. I didn't feel like myself until seven months after my surgery. I went through a period of depression, which doctors don't always talk about. I still live with fear of having a heart attack. I want to see heart disease get the attention it deserves."



THE NO. 1 KILLER

According to the American Heart Association, cardiovascular disease claims the lives of more women than the next four causes of death combined – almost twice as many as all forms of cancer. Yet,

a survey commissioned by the Society for Women's Health Research found that, while women's fear of heart disease has almost doubled since 2002, breast cancer continues to be the most feared disease.

"While 49 percent of women now know the No. 1 killer in women is heart disease, if you ask them if the risk factors apply to them, only 13 percent say yes. We're doing a good job of getting the word out, but we're still not getting through to them that this applies to you, not the lady sitting next to you," said Lisa Mendes, M.D., assistant professor of Medicine at the Vanderbilt Heart and Vascular Institute.

Cardiovascular disease typically presents in women 10 years later than it does in men, at about age 70, although women can certainly have heart attacks much younger. Mendes said that conventional wisdom suggests that female hormones may protect the heart, and when they are depleted, a woman's risk becomes the same as a man's. Heart disease actually starts developing during the teenage years and early 20s, although it may not show up until much later. For this reason, early prevention is the key.

Jim Atkinson, M.D., Ph.D., professor of Pathology at VUMC, conducted a study called the "Pathologic Diagnosis of Atherosclerosis in Youth," which revealed a great deal about the progress of atherosclerosis and its natural history. Researchers examined blood vessels of young people who died from non-cardiovascular causes. What was clear was that both groups already had the early stages of atherosclerosis in their blood vessels, boys in their teens and young women in their 20s.

"The bottom line is this is a disease that starts in youth," Mendes said. "By the time you are in your 40s the disease is already there. The thing to remember is, start prevention in your 20s, not in your 60s when you're having your first heart attack."

Middle-aged women often care for others more than themselves. They don't take the time to assess their health risks

According to the American Heart Association, cardiovascular disease claims the lives of more women than the next four causes of death combined — almost twice as many as all forms of cancer.

because they are busy working, raising children, and taking care of aging parents.

“There are a lot of factors in women’s lives that make it harder for them to focus on their own health. They do need to be aware of that and do the things the American Heart Association has outlined in terms of preventing and reducing their risk of developing coronary disease,” Mendes said.

The first step in preventing heart disease is to know your risk. The Framingham Heart Study has played an important role in establishing risk factors, which include age, cholesterol (total cholesterol and HDL), systolic blood pressure, whether or not the patient uses medical treatment for hypertension, and cigarette smoking. It estimates the risk of developing coronary heart disease within 10 years.

♥ ♥ ♥ A NEW APPROACH

In February 2007, the American Heart Association developed new guidelines and encouraged health care professionals to focus on women’s lifetime heart disease risk, not just short-term risk.

“Women have had the notion that they are safe and off the hook until they get to menopause, and then they can start paying attention to some of these issues like cardiac risk factors,” said Rose Marie Robertson, M.D., past president and current chief science officer of the American Heart Association and professor of Medicine at VUMC. “What we know through studies done at Vanderbilt and elsewhere is that the concept of waiting is really a bad idea and misses the boat.”

The updated guidelines include a new paradigm for risk assessment based on risk factors and family history, as well as the Framingham risk score. A quick glance at the risk factors brings a startling realization: nearly all women have some level of risk for cardiovascular disease. According to the American Heart Association, in the United States 42.1 million (36.6 percent) women live with cardiovascular disease and one in three women will die from it.

“By looking at people’s lifetime risk, including family history and all of the other known risk factors, these guidelines provide a more reasonable way to give women the best advice about what they ought to be doing,” Robertson said.

♥ ♥ ♥ PREVENTION IS THE KEY

According to AHA literature, the 2007 update provides the most current clinical recommendations for preventing cardiovascular disease in women 20 and older (see sidebar). The guidelines focus on weight control, smoking cessation and low dose aspirin therapy and are based on a systematic search of the highest quality science interpreted by experts in the fields of cardiology, epidemiology, family medicine, gynecology, internal medicine, neurology, nursing, public health, statistics and surgery.

Emily Kurtz, M.D., assistant professor of Medicine at the Vanderbilt Heart and Vascular Institute, did her cardiology training at Vanderbilt but also spent a year at the Brigham and Women’s Hospital in Boston, where she received subspecialty training in preventive cardiology and

Quick Facts

♥ HEART DISEASE & STROKE ♥

1. Only 13 percent of women view heart disease as a personal health threat, even though it’s women’s No. 1 killer.
2. Cardiovascular disease (CVD) kills 480,000 women a year, about one per minute.
3. One in three adult females and males in the United States suffers from a form of CVD.
4. CVD claims more lives of women than the next four most common causes of death combined.
5. On average, an American dies of CVD every 35 seconds.
6. Coronary heart disease is the No. 1 single killer of women over age 25.
7. Sixty-four percent of women who died suddenly of coronary heart disease had no previous symptoms.
8. One in 2.6 female deaths are from CVD, compared with one in 30 from breast cancer.
9. Heart disease rates in post-menopausal women are two to three times higher than in pre-menopausal women of the same age.
10. Stroke is the No. 3 cause of death for American women, and is a leading cause of serious, long-term disability.
11. Stroke kills more women than men. In 2003, females represented 61 percent of stroke deaths.



Lisa Mendes, M.D., top, and Emily Kurtz, M.D., bottom, are leading Vanderbilt Heart and Vascular Institute's efforts in women's heart health and prevention.

collaborated with the Women's Health Study investigators. She now has a leadership role in implementing a cardiovascular prevention and treatment center at Vanderbilt's One Hundred Oaks medical campus, scheduled to open next year.

"Most people believe you don't need to see a cardiologist until you develop angina or have had a heart attack. As a preventive cardiologist, my interest is in identifying predictors of risk in people who have not yet had a cardiac event," she said.

The strategy of the cardiovascular prevention center will be to provide a comprehensive cardiovascular risk evaluation as recommended by the AHA, evidence-based cardiovascular screening and diagnostic testing, and early detection and management of cardiovascular risk factors using aggressive lifestyle and/or medical management, all with the intention of decreasing cardiovascular risk; slowing the progression of atherosclerosis in the heart, peripheral blood vessels, and brain; and

No more... "*Dear, you need a hysterectomy*"

Uterine fibroids affect most American women over 50, but there is surprisingly little evidence to help compare standard treatment recommendations, according to a recent report.

Uterine fibroids are non-cancerous growths of the uterus that cause symptoms in about half of the women who have them. Concerns may include heavy bleeding, pelvic pain, backaches, bowel and bladder function changes, and painful intercourse.

They affect more than 80 percent of African-American women and nearly 70 percent of white women in the United States by age 50.

The lead clinical author of the report was Katherine Hartmann, M.D., Ph.D., deputy director of the Institute for Medicine and Public Health at Vanderbilt University Medical Center and vice chair for Research in the Department of Obstetrics and Gynecology, who was at the University of North Carolina at Chapel Hill when the research began.

The solution for decades has been "dear, you need a hysterectomy," Hartmann said.

"The body of knowledge from the literature is strikingly limited. Considering that millions of women in the U.S. have fibroids, there has been completely inadequate research attention and funding focus on high quality research in this area."

Hartmann and colleagues examined 107 studies conducted on the topic between 2000 and 2006.

Current treatment for uterine fibroids varies in terms of invasiveness and cost. The report says that there has been woefully little research comparing the risks and benefits of different treatment options, and few pharmaceutical options for symptom relief have been studied for long-term effectiveness.

The report did show that women who received a uterine artery embolization, a newer non-surgical treatment that shrinks the fibroid, had shorter hospital stays and a quicker

most importantly, preventing or delaying the onset of a first cardiovascular event, such as a heart attack, stroke, or even death.

In addition to screening patients using traditional risk markers, such as diabetes, high blood pressure, smoking, and high cholesterol, the cardiovascular prevention and treatment center at One Hundred Oaks will also offer novel testing, such as non-invasive imaging (like coronary CT angiography) to diagnose subclinical (before the onset of symptoms) atherosclerosis, endothelial function testing to assess the health and function of the blood vessels, and serum biomarkers of inflammation, which contribute to the development of atherosclerosis and increase the likelihood of rupture of vulnerable plaque. In addition to establishing care with a cardiologist, consultations with a registered dietitian and exercise physiologist will be offered, and referral to other subspecialty physicians (such as endocrinologists and neurologists) will be arranged as needed.

“We plan to emphasize the evaluation and appropriate assignment of CVD risk in women and will prioritize preventive interventions, ranging from dietary and physical activity recommendations to medical management, further diagnostic testing, or invasive procedures, based on

these risk classifications,” Kurtz said.

Women go through unique periods in their lives – adolescence, pregnancy and menopause. The kind of physiologic responses a woman has to those unique periods may help predict her risk of developing cardiovascular disease, both in the short and long run.

For example, if a woman has preeclampsia in pregnancy, there is strong evidence to suggest she is at higher risk for developing hypertension and cerebrovascular disease, Kurtz said. There is also recent evidence to suggest that women who have migraine headaches with visual symptoms (or aura) may be at increased risk for stroke compared to women who do not have migraines, researchers reported in *Stroke*, a journal of the American Heart Association, a division of the AHA.



MORE STUDIES NEEDED

Studies conducted in the 1970s and 1980s looked at coronary disease in men specifically. As it became clearer that women’s risk of cardiovascular disease and mortality associated with it was quite high, there has been more emphasis in the

past decade to include women in studies, although this hasn’t been as successful as it was intended to be. As Robertson notes, women weren’t excluded on purpose. Often they were left out from studies based on inclusion criteria, such as age, or because of concern about risks.

“If you’re including women of childbearing age, there aren’t as many who have had a heart attack as there are men,” Robertson said. “And any drug you give to a woman of childbearing age, you’re now potentially giving to a fetus, too.”

While much progress has been made in the prevention and treatment of cardiovascular disease in women, much work remains to be done.

“You never talk to any of us who don’t say we need more research. I think we have made huge strides in the research endeavors that we have done. But there are still so many things we don’t know on the other hand,” Robertson said. “I think there is extraordinary good news for women even now. Science and medicine and education awareness have combined so we know about risk factors, and we have the therapeutic ability to treat them. If we just do those things we know need to be done, we can have a huge impact. It can be done; we just have to have the will.” **VM**

recovery than those who received a hysterectomy or myomectomy, which removes the fibroids without removing the uterus.

But few studies compared complications, long-term symptom relief or looked at the choice of either treatment with other treatments.

There was also little evidence of long-term symptom improvement with MRI-guided ultrasound ablation of fibroids, another new treatment that uses high intensity, focused ultrasound waves to destroy the fibroid tissue.

Another area of concern, and an area of focus in the report, is women with fibroids who are considering becoming pregnant, especially those who have had a miscarriage or who are having trouble with infertility.

These women get fairly pointed advice from their gynecologists that they should consider surgery, Hartmann said.

“But in this review, we’re saying that there’s just not

enough evidence to make that suggestion except in one instance — women with fibroids that are jutting into or in contact with the uterine cavity,” she said.

“How did we get to the point where 20 to 50 percent of women in their reproductive age are going to have fibroids and we have no medical management strategies, we have very limited direct comparison of surgical intervention, and we can’t even advise women what they ought to do about their reproductive function with respect to fibroids, with the exception of about 10 to 20 percent of women who have fibroids in the uterine cavity?” Hartmann asked.

—NANCY HUMPHREY



THE Swirling

DEBATE AROUND HORMONE REPLACEMENT THERAPY

WRITTEN BY ELIZABETH OLDER
ILLUSTRATION BY JODY HEWGILL

The bad news about the risks of long-term hormone replacement has left some women all hot and bothered – and not in a good way.

In the wake of the watershed results of the multimillion-dollar, long-term Women's Health Initiative (WHI) study, women suffering bothersome menopausal symptoms are left swirling in pros and cons, more carefully weighing the risks and benefits of using hormone replacement to bring some normalcy back into their lives. And this decision has been made even more confusing by the fact that the WHI didn't actually address the use of short-term hormone replacement to help women through the so-called "change of life."

"The Women's Health Initiative was a prevention study," explains Esther Eisenberg, M.D., M.P.H., professor of Obstetrics and Gynecology. "It was not a treatment trial."

The estrogen-plus-progestin combination that for decades has been a frontline of defense against menopausal symptoms was dealt a blow in 2002 when the massive WHI stopped study trials on the common hormone replacement regimen. The project's primary focus was to determine if hormone replacement prevented a number of chronic diseases in post-menopausal women. But this part of the randomized clinical trial was halted early when it became apparent that the opposite effect was occurring: study participants taking the estrogen-plus-progestin combination were suffering more breast cancer, heart

attack, stroke and blood clots than the group taking a placebo. And an ancillary study showed hormone use increased the risk of dementia in women 65 and older.

"All of a sudden you had a huge number of women stopping their hormones without talking to us," recalls Eisenberg. Even though the WHI was not meant to evaluate the risks and benefits of the short-term use of hormone replacement to alleviate menopausal symptoms, the startling study results prompted some women to stop taking the medication for that problem and others to avoid starting it, says Eisenberg. But some patients – struggling with night sweats, hot flashes, vaginal dryness and other bothersome symptoms – stuck with the treatment, she says.

Using hormone replacement to help alleviate menopausal symptoms – a use it was approved for by the U.S. Food and Drug Administration – requires the physician and patient to look at the balance between benefits and risks, says Eisenberg. She sees the threat of increased disease for an individual woman using hormones for this reason as "very low."

"Women who have symptoms want to feel better," she says, adding that taking hormone medication still is the most effective treatment for many people.

Science trumps the common wisdom

Up until the WHI trial the combination of estrogen-plus-progestin had achieved something akin to anointment

as a magic potion for post-menopausal women. The results of some observational studies, in which groups of women taking and not taking hormones reported their lifestyle and health experiences, touted it as a potential protective against cardiovascular disease and dementia. These findings elevated hormone replacement during the 1990s into the category of a prescription that prevented disease, far beyond its FDA-approved use to control debilitating menopausal symptoms and ward off the bone-thinning disease osteoporosis. By the mid-1990s, physicians' professional organizations and the American Heart Association supported the recommendation of hormone replacement to older women for both heart and bone health. By 2001, millions of women had hormone prescriptions, and many were older women taking the pills solely to promote better health and long life.

But Lisa A. Mendes, M.D., assistant professor of Medicine at the Vanderbilt Heart and Vascular Institute, says some studies prior to the WHI had narrowed the window for using hormone replacement for heart health. The Heart and Estrogen/Progestin Replacement Study (HERS) reported in 1998 that the use of estrogen-plus-progestin in post-menopausal women with previous heart disease did not prevent another heart attack or death from heart disease, but did raise the risk of blood clots and gallbladder disease.

68,132
 NUMBER OF
 POST-MENOPAUSAL
 WOMEN AGE 50 TO 79
 ENROLLED IN
 WHI-RANDOMIZED
 HORMONE THERAPY
 TRIALS

“The results of this study were completely opposite to what the investigators expected,” Mendes said.

Then in 2002 the WHI, the first large randomized prevention study, provided a bigger picture, reporting that estrogen-plus-progestin did lower the risk for developing osteoporosis, since fewer hip and other fractures were reported. Taking the hormones also was linked to a reduction in risk for colorectal cancer. However, the risk of breast cancer, heart attack, stroke, and blood clots in the legs and lungs were all higher among the women taking the hormones, as was dementia in women 65 and older.

“The risk was generally small, but it was still a real difference,” says Mendes. “I think it was a shock to a lot of people.”

And while a companion study found that middle-aged women without a uterus taking estrogen alone may be able to use the drug without incurring increased risks for breast cancer and heart disease, Mendes says she believes the days of suggesting hormone replacement as a heart-healthy prescription probably are past.

Hormone use drops and so does breast cancer

The results of the WHI study shook up a lot of women taking the drugs. But perhaps even more startling was what happened when millions of women abandoned the drug regimen after that news broke in 2002.

The annual incidence of breast cancer dropped dramatically in the two years after the WHI study was halted, when millions of women stopped taking the hormones. Researchers have linked the disease decline, particularly in estrogen receptor-positive breast cancers, to the drop in hormone use, and are continuing to monitor the statistics to learn more about the trend.

Julie Means-Powell, M.D., of the Vanderbilt-Ingram Cancer Center, says research on breast cancer already had hinted at a link to higher levels of estrogen and other hormones naturally produced in the body. Post-menopausal women who have

breast cancer tend to have higher levels of endogenous estrogen, she says. The same is true of women who have more menstrual cycles in their lives – therefore, a longer exposure to hormonal fluctuations.

“So, obviously, women who take hormone replacement increase their exposure to estrogen,” says Means-Powell, a medical oncologist and assistant professor of Medicine in the Division of Hematology/Oncology. “I don’t think it was surprising.”

Even though the incidence of breast cancer declined, she says some people aren’t convinced that can be attributed to the precipitous drop in hormone use. But Means-Powell anticipates an even further decline as behavior continues to adjust in light of the WHI findings.

“It was important information,” she says. “It sort of changed the paradigm of how we approach post-menopausal women.” As for her cancer patients, they continue as before to be counseled against taking hormones if they have had estrogen receptor-positive tumors or a family history or disease profile that suggests an increased risk for developing breast cancer. As for others, she suggests hormones should have limited usage for a targeted population.

No new insight into short-term hormone use

Since she has a special interest in treating patients with difficult menopausal symptoms, Eisenberg has been in the eye of the WHI storm. Even though the study was not designed to evaluate the risks and benefits of short-term hormone replacement to relieve menopausal symptoms, the well-publicized results have complicated the decision for many women.

“Some women who were concerned stopped their medication. Some women said they didn’t want to go on hormones,” she explained. But other patients, suffering debilitating menopausal symptoms, want to take hormone replacement, she says.

“When you have symptoms you have a different balance of benefits and risks,” she says.

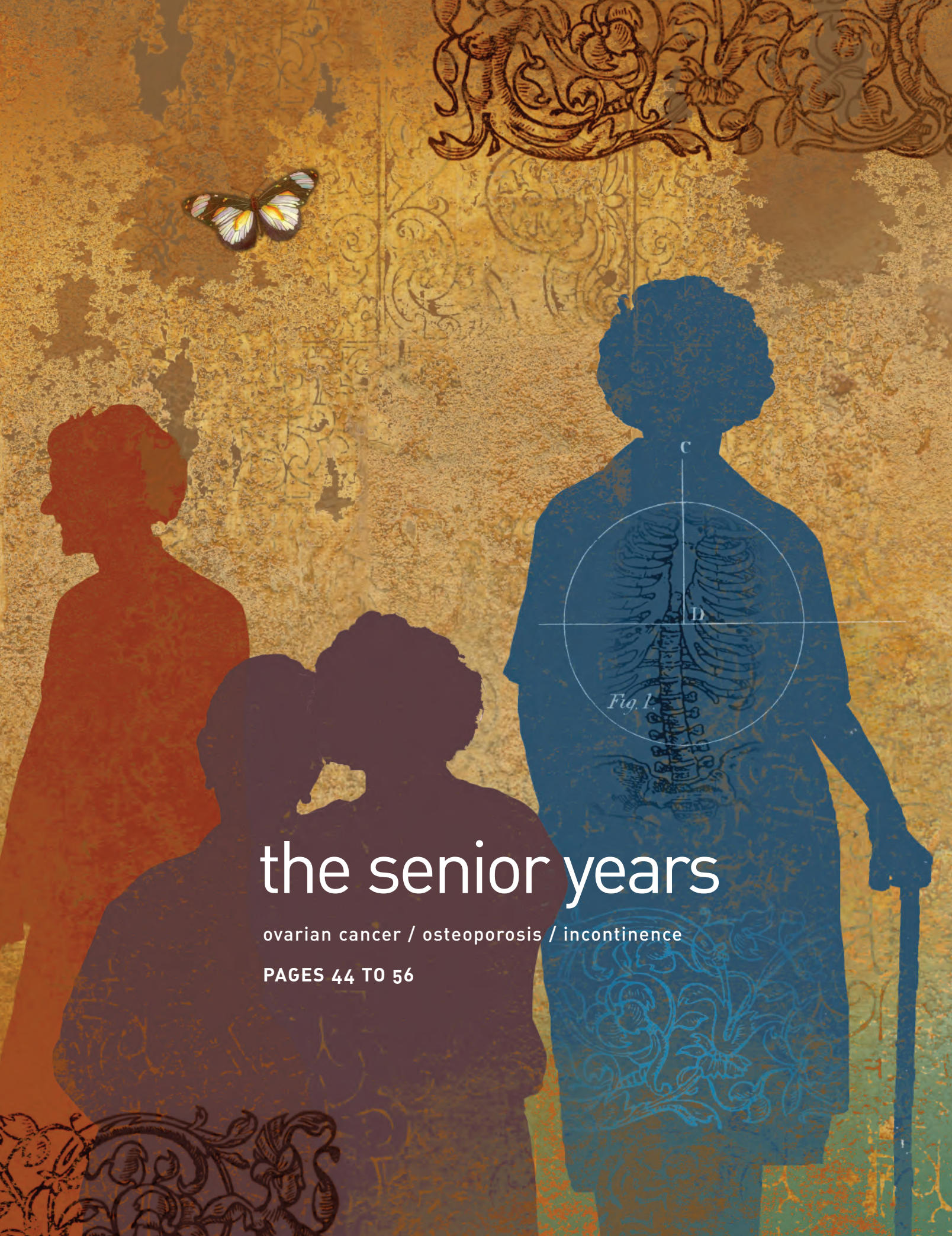
The WHI-randomized hormone therapy trials enrolled 68,132 post-menopausal women from 50 to 79. The hormone used was the most commonly prescribed pill form of estrogen-plus-progestin, which leaves unanswered questions about the possible disease preventive benefits of hormone replacement using other delivery methods, dosage levels and treatment formulations.

The safety and effectiveness of alternative nonprescription supplements for “change of life” symptoms – such as soy-based products, botanical black cohosh and red clover – have not yet been proven. And bioidentical hormones – formulated to have the same chemical structure as the hormones made by the human body – also have not been conclusively studied. These compounds are made by pharmacists for each individual based on hormone deficiencies identified through saliva samples.

Research is under way to learn more about some of these alternative treatments and supplements. These alternatives are not under the oversight of the FDA, although the mainstream drug industry is pushing for regulatory intervention from that agency.

So, for now, as the FDA guidelines counsel, Eisenberg advises patients who need relief from menopausal symptoms to take the lowest effective hormone dose for the shortest possible time. The target use is no more than five to seven years. She tells her patients they can reassess the prescription over time and reduce the dosage or stop the treatment if it’s no longer needed.

“The decision must be made one patient at a time, thinking about the individual patient in front of you,” she said. **VM**



the senior years

ovarian cancer / osteoporosis / incontinence

PAGES 44 TO 56





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Harriet Foley always believed her greatest health care threat would be heart disease. After all, her family tree includes several branches with relatives who died from cardiac illnesses, including her mother. So the longtime Nashville resident was shocked when her physician discovered another life-threatening illness – ovarian cancer.

“I was having a routine physical and the doctor touched a spot on my lower abdomen, and I almost jumped off the table,” Foley remembers. “My doctor told me he wanted me to have an ultrasound, and he made the appointment for me. But it didn’t suit me because I knew perfectly well it wasn’t my destiny to die of cancer; I was going to be a vascular patient.”

ed to keep that initial
: Burnett, M.D.,
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e Foley kept the

appointment and underwent an ultrasound examination which revealed a mass in one of her ovaries.

“Dr. Burnett called and told me it didn’t look good and he had made an appointment with the best oncologist in town.” Vanderbilt’s Howard Jones III, M.D., one of the best-known gynecologic oncologists in the country, performed further tests and decided to operate. He discovered Foley had stage III ovarian cancer which required surgical removal of the ovaries followed by chemotherapy.

Since the 83-year-old Foley had been focused on the risk of heart disease, she didn’t realize her age also made her a prime candidate to develop cancer of the ovaries – two walnut-sized reproductive organs that sit on either side of the uterus in the lower abdomen. According to the National Cancer Institute, 50 percent of all women with ovarian cancer are over the age of 65, but younger women can also be affected.

It is post-menopausal women like Foley who are most likely to develop tumors in the epithelial cells covering the

Quick Facts on cancers affecting women

1. Breast cancer

Breast cancer is estimated by the National Cancer Institute to affect 178,480 women in 2007, causing 40,460 deaths.

Vanderbilt-Ingram Cancer Center is one of the research centers which has received a Specialized Programs of Research Excellence (SPORE) grant from NCI for breast cancer research. The five-year, \$13 million grant funds translational research – laboratory-based research which can be applied in the clinical setting.

Carlos L. Arteaga, M.D., principal investigator and director of the Breast SPORE, said work is promising in estrogen receptor-positive breast cancer – so-called (ER)-positive breast cancer – and HER2-positive breast cancer, cancers with amplification of the HER2 gene.

But some kinds of breast cancer are still baffling to scientists – specifically breast cancer called triple-negative or of the basal type. Nearly 10 percent of all breast cancers are triple-negative and they are most prevalent in minorities.

“Those tumors don’t have detectable hormone receptors so hormonal therapies don’t work. They don’t depend on HER2, so known treatments don’t work against them. In those tumors we have little understanding of what critical molecules are driving the cancer,” Arteaga said.

outside of the ovary. Nearly 90 percent of all ovarian cancers are epithelial cancers which can be notoriously difficult to treat in late stages.

Foley’s referral to Jones, director of the Division of Gynecologic Oncology, ensured she would receive a treatment regimen that gave her a fighting chance of surviving the often-deadly disease because with ovarian cancer, more than many other forms of cancer, what you do first matters.

That first step usually entails surgery to identify and remove the tumors. Several recent studies indicate patient prognosis is improved when the initial surgery is performed by a specialist with expertise in cancer surgery. Intensive training enables these surgeons to remove more of the cancerous tumors which often spread beyond the ovary into the abdominal cavity.

“Whether it’s early disease or advanced disease several studies show patients have better survival with gynecologic oncologists,” Jones said. “We’re more aggressive and we give chemotherapy in a more integrated way because most of the time gynecologic oncologists give their own chemotherapy. It’s an integrated form of treatment from the start.”

At Vanderbilt that integrated treatment is provided by a team of specialists in several medical disciplines who meet every week to discuss and manage each patient’s case. Surgeons confer with pathologists, radiation oncologists and others to determine how best to treat each patient, some of whom have genetic precursors that make them vulnerable to ovarian cancer.

A very opportunistic disease

Even with the best initial treatment ovarian cancer remains one of the most deadly forms of malignancy. The National Cancer Institute estimates 22,430 new cases of ovarian cancer in the United States in 2007, with 15,280 deaths. While ovarian cancer is not the most common of the gynecologic cancers, it is the most common cause of death

among women who develop cancer of the reproductive organs.

“If we catch ovarian cancer when it’s confined to the ovary at stage I we can cure about 90 percent of those women, but the problem is we don’t often catch it when it’s stage I,” said Marta Crispens, M.D., assistant professor of Obstetrics and Gynecology at VUMC.

Nearly 75 percent of the time ovarian cancer patients are diagnosed when the disease has already advanced to stage III or stage IV. The reason: ovarian cancer has few warning signs during early stages of the disease. Sometimes patients report no symptoms at all. Other times those symptoms can be as subtle and quiet as leaves rustling softly in the breeze...and as easily dismissed by women and their physicians. Pain or swelling in the abdomen, pain in the pelvis and gastrointestinal problems such as gas, bloating or constipation are signs of ovarian cancer, but they can also be symptomatic of other milder health care problems. Women who are aging may write off that lower abdominal “pooch” as one of the less desirable, but sometimes inevitable, side effects of menopause.

But ignorance in these cases isn’t bliss – it can be dangerous. Unlike breast cancer which has been the subject of a massive public education campaign urging women to check their breasts and get regular mammograms, most women don’t know what to look for, so ovarian cancer manages to sneak up quietly and deliver an unexpected blow.

Harriet Foley had blamed the slight pain in her abdomen on a tight undergarment.

“I wore a girdle and I thought the tender spot was where the girdle was too tight. I had that slight pain for at least a month before I went in for my routine physical.”

Time was not on her side. While her gynecologist quickly ordered additional tests when he discovered her painful response to the pelvic exam, all too often women and their physicians don’t investigate the cause of those symptoms early in

Nearly 70 percent of the time ovarian cancer patients are diagnosed when the disease has already advanced to stage III or stage IV.

the disease progression. That allows the cancer time to spread beyond the ovary, and ovarian cancer is a very opportunistic disease.

“Cancer of the ovary flakes off the surface of the organ,” said Jones. “It can go to the lymph nodes through the lymphatic channels. It can go to the lungs through the venous channels, but mostly what it does is flake off, and the cancer cells float around in the abdomen. The omentum, the fatty apron that hangs down from the stomach, sweeps up all of these cancer cells and they start growing. There’s good blood supply in the omentum, which makes it an ideal environment for tumor growth.”

Ovarian cancer also may metastasize to the liver or other organs within the abdominal cavity, so surgery to remove it may be extensive.

“If I’m able to get most of the tumor out then I can tell that woman she has a three out of four chance of achieving a remission which means seeing all of the clinical signs of cancer go away,” said Crispens. “Unfortunately, while we’re very good at achieving remission we’re not so good at keeping people there. What happens is that most women will eventually recur. The median time to recurrence is about two or three years and at that point a woman may be on chemotherapy the rest of her life.”

Turning the shark loose

Harriet Foley was determined to be one of those patients with a hopeful outcome. “The first time I met Dr. Jones I told him I felt like I had all of these little fish swimming around in me, which of course were the cancer cells, and he told

me he was getting ready to turn a shark loose on them.”

That shark was chemotherapy. “I immediately visualized something swimming around and eating those little fish and to me the chemo became the shark, and I would say ‘I’m going to go back and get some more shark.’”

During her treatment sessions Foley started writing what she calls doggerel and much of the writing focused on that shark, which she named Ishmael, a reference to Hermann Melville’s “Moby Dick.”

In Foley’s prose the epic battle pitted her against a wily and aggressive shark instead of a whale. “He certainly had his way. One bite and he took my hair.”

While the chemotherapy “shark” was gobbling up her hair, it was also attacking her cancer. “The silver lining here is that ovarian cancer is one of the few cancers that may respond well to chemotherapy,” explained Jones.

Oncologists typically recommend, and the FDA has approved, several chemotherapy drugs, often used in combination, to treat ovarian cancer. Two of the most commonly used are Paraplatin (carboplatin) and Taxol (paclitaxel). Taxol was approved in April 1998 as a first-line treatment for advanced ovarian cancer. It has been used since 1992 to treat advanced ovarian cancer that has not responded to other therapies or that has progressed after treatment.

Several recent clinical trials have tested a new way to deliver the chemotherapy directly into the peritoneal cavity through a catheter. While survival improved, so did toxicity for the patients, and there were several problems with the catheters

2. Lung cancer

Lung cancer traditionally has been considered a man’s disease, but the disease now kills nearly twice as many women as breast cancer.

“There’s a feeling it’s a self-inflicted cancer, which is incredibly unfair since cigarettes are legal and highly addictive, and especially unfair to the nearly 20,000 people per year who take care of themselves, never smoke, and get lung cancer anyway,” said David Carbone, M.D., Ph.D., Harold L. Moses professor of Cancer Research and director of the Thoracic Oncology Center.

Even people who smoke for a few years and later quit can develop the disease decades later due to the permanent genetic damage smoking causes. Lung cancer is also highly lethal, with only about 15 percent of people diagnosed alive five years later.

Carbone is particularly excited about the 2007 renewal of Vanderbilt-Ingram Cancer Center’s SPORE in Lung Cancer grant from NCI, which he directs. Much of the research in that SPORE is focused on finding a blood test for lung cancer.

3. Colon cancer

Colorectal cancer is the third leading cause of cancer death in the United States and until age 50 women are nearly as likely as men to develop the disease. Modest decreases in colorectal cancer deaths in the past decade have been attributed to the detection and removal of precancerous growths or polyps, early detection of tumors through screening and improved treatments.

One of the best screening tests is a colonoscopy, however, the

invasive nature of a colonoscopy makes some patients unwilling to undergo the screening test which is recommended for everyone at age 50 and even earlier for those with risk factors like a family history of colon cancer. So researchers at Vanderbilt-Ingram Cancer Center are trying to develop a simple blood test to screen for the disease.

"I think in the next five years we will be able to identify proteins that are indicative of cancer, and we will be able to detect many of these markers in the blood," said Daniel Liebler, Ph.D., director of the Jim Ayers Institute for Pre-Cancer Detection and Diagnosis.

4. Cervical cancer

The most important news about cervical cancer in women is that it may be preventable. Scientists have discovered most cases of cervical cancer are caused by the human papillomavirus (HPV), one of the most common sexually transmitted diseases. The FDA has now approved a vaccine for girls and young women which prevents the HPV infection that leads to cervical cancer.

Physicians are using colposcopy to identify abnormal blood vessel patterns on the superficial epithelium of the cervix. When serious abnormalities are found, the cells are removed through large-loop excision – a wire loop that cleanly removes the affected tissue, said Howard Jones III, M.D., director of the Division of Gynecologic Oncology.

For more information on women and cancer visit www.vicc.org/women.

delivering the drugs into the abdomen. Now researchers are trying to determine the optimal dosage levels for treatment and are exploring methods to keep the catheters from clogging.

For women the question remains – who is at risk for ovarian cancer? Advanced age is just one of the risk factors. Approximately 10 percent of women with ovarian cancer have a hereditary predisposition to develop the malignancy because they carry mutations in certain genes – the BRCA1 and BRCA2 genes – that make them susceptible to both ovarian and breast cancer. For those women, an oophorectomy (removal of the ovaries) is a preventive option.

For other women taking birth control pills can decrease the risk of ovarian cancer. The pills prevent ovulation, and researchers suspect the process of ovulation makes ovarian tissue susceptible to cancer-causing agents. Like many other forms of malignancy, scientists still don't know what causes ovarian cancer. Researchers believe a mutation in the COX2 gene may play a role because it is linked to inflammation. Mutations in certain proteins also may be tied to tumor development.

While scientists try to unravel these clues, researchers at Vanderbilt are focused on a test that could save more women who actually develop the disease. "I think by the time people get advanced cancer there are so many things going on in those cells that is so disruptive and is so basic to the function of the cells that maybe that's the wrong target," said Crispens. "Maybe the target truly is to find it early. I'd like to tell women that we can screen for ovarian cancer."

Such a screening test would finally give women and their doctors some warning that ovarian cancer is present, but developing a reliable screening test has been complex. Physicians often order a CA125 blood test which measures the amount of a specific protein circulating in the blood. While the test is useful in assessing disease progression in women

who have undergone cancer treatment, it is not considered a reliable screening tool by most experts. The test is negative in many women with early disease while it is often elevated in women who don't have cancer, which means too many women with an elevated CA125 may undergo unnecessary surgery.

Seeing is believing

To avoid unnecessary surgeries and in the absence of a blood test, researchers at Vanderbilt have turned to imaging as a tool to detect ovarian cancer in its earliest stages. For 25 years Arthur C. Fleischer, M.D., professor of Radiology and Radiological Sciences has been trying to find a way to provide that early warning system to ovarian cancer patients. "The classic case is Gilda Radner," said Fleischer. The actress and comedienne best known for her "Saturday Night Live" sketches may be the most public face for this disease. "She had several genetic risk factors but it wasn't until she was undergoing surgery for infertility that they discovered ovarian cancer." After Radner's death her husband, actor Gene Wilder, launched a foundation in her honor which includes "Gilda's Club," a network of local cancer support organizations which provide education and counseling for cancer patients.

To aid current and future generations of women like Radner, Fleischer and other Vanderbilt researchers have been using a new type of specially tuned transvaginal sonography and a newly developed intravenous contrast agent made up of microbubbles to study changes in the blood flow patterns in tumors to identify possible ovarian cancer. Tumors are well-known for recruiting new blood supplies in a process called angiogenesis. "In normal tissue you have a very orderly branching of blood vessels," explained Fleischer. "You have a big artery going to a smaller artery then branching into a capillary. But in tumors you have these microscopic webs of capillaries that are abnormal, and the blood



Harriet Foley at home
in her favorite chair

TAMARA REYNOLDS

*My name is Ishmael,
I'm the great white shark
Cast by Dr. Jones
Into my Hostess' lair
To catch the tenacious C-Cells
Swimming there.*

*She cried, "Yes", "Whoopee", "Right on",
Until she found
I was going to eat her hair!*

— HARRIET FOLEY, 2005

flow pattern and flow dynamics are quite different.”

Fleischer, working with Vanderbilt's Andrej Lyshchik, M.D., Ph.D., has been developing an intravenous contrast agent using inert microbubbles that are smaller than a red blood cell to highlight these changes. “It starts with a solution that gets shaken up that produces the microbubbles. We draw the solution up into a tiny syringe and inject them into an arm vein, followed by a small volume of normal saline. Then we use a specially tuned transvaginal sonographic probe to track the progress of the solution and those microbubbles as they literally light up the screen – it turns white when there is a network of abnormal blood vessels in a tumor. We can see the difference

between vascularity in normal tissue and abnormal vascularity in tumors.”

In the study supported by a grant from the National Cancer Institute, part of the National Institutes of Health, Fleischer and his colleagues have tested this technique in 19 patients and have established significant differences in microvessel flow between benign and malignant ovarian tumors.

Despite these exciting advances in imaging, Fleischer believes a blood test is still the best option for an initial screening tool of the general population, with sonography best utilized in women with pelvic masses or those considered high risk. Researchers across the country are using proteomics – the study of proteins to determine which proteins are over-expressed in

various cancers. Measuring those proteins in the blood could be the first step in determining which patients need a contrasted pelvic sonogram to determine if they have a tumor and hopefully to detect an ovarian cancer in its earliest stage.

For patients who do have cancer, researchers are opening clinical trials to test new drugs that block angiogenesis, without some of the side effects exhibited by current angiogenesis inhibitors.

Crispens, the gynecologist, is both touched and amazed by the women who have volunteered for these and other clinical trials to find life-saving treatments for this disease. To ensure the results are scientifically valid, the best trials are randomized and require a control group. “To think that you would commit yourself to come here for a year and a half is a really difficult thing to ask somebody to do. On the other hand, that's how we make the strides forward and how we know the new drugs work in some cancers. It's a big sacrifice for patients to make, and we're grateful to them.”

Harriet Foley, whose lovely white hair has returned, exhibits that grace and courage. She believes her sense of humor and the therapy of writing about her illness have helped her cope with her diagnosis. “You can't let it ruin your life. At my age you know each day is a gift,” a gift made more poignant by a life-threatening illness. **VM**

*“You can't let it ruin your life.
At my age you know each day is a gift.”*

BAD to the BONE

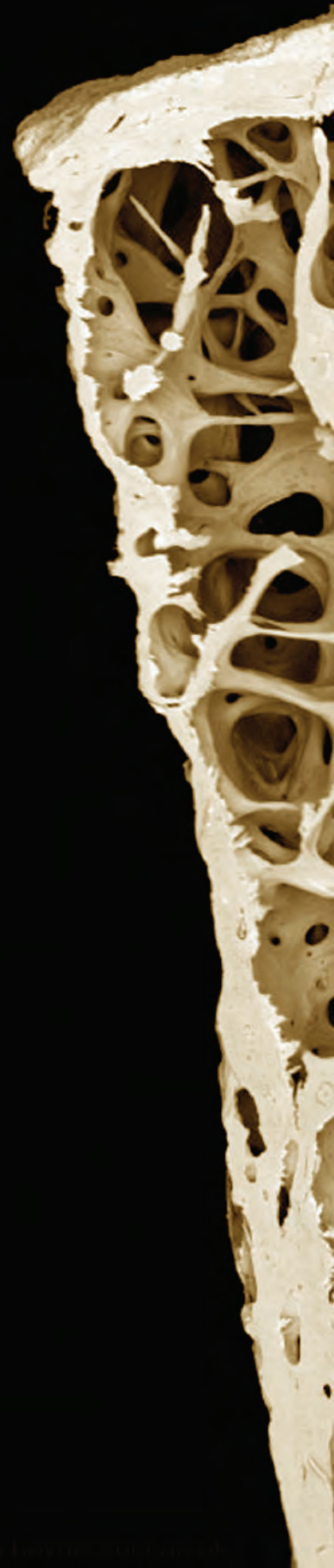
Bone may be the hardest, most durable substance in the body, but it's not indestructible. There's a thief at large – the disease osteoporosis – slowly and silently draining bones away until they weaken or snap.

As life expectancy continues to climb, both women and men face the increased possibility of pain and disability caused by the insidious disease, which causes bone to become porous and fragile, leading to an increased risk of fractures.

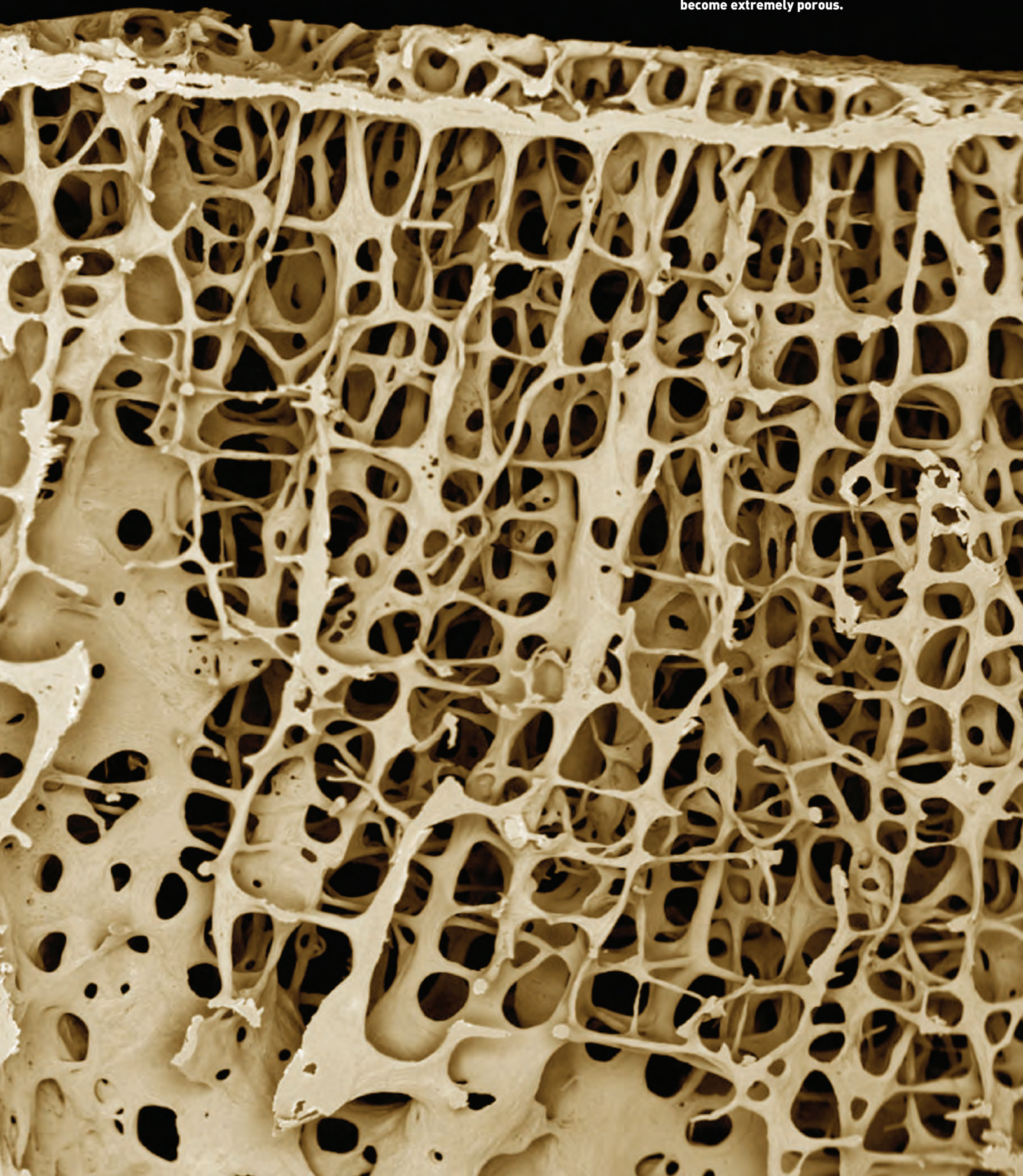
But women are much more likely to develop this condition during the time of menopause and the first years beyond as they lose more and more of the protective effect of natural estrogen, while men tend to lose more slowly, catching up with women by age 65 or 70.

"We're living to be 10 years older than our parents and grandparents," says Gregory Mundy, M.D., the first John A. Oates Chair in Translational Medicine and director of the Vanderbilt Center in Bone Biology. "Many of us are going to live well into our 80s and 90s, and some of us longer." As a result, he explains, many otherwise healthy adults face the very real possibility of being "crippled by their bones," a fate that Mundy and other researchers hope to avert by developing a better understanding of osteoporosis and new methods to prevent and treat it.

WRITTEN BY ELIZABETH OLDER
ILLUSTRATION BY GETTY IMAGES



The bones of an 89-year-old woman with osteoporosis, a disease in which bones become extremely porous.



The relationship between aging and increased bone fragility has long been recognized in medicine. But it was only in 1994 that a group of World Health Organization experts first quantified the criteria that defined osteoporosis as a disease.

“That was really a big impact on the field,” says S. Bobo Tanner, M.D., an assistant professor of Medicine in the Division of Rheumatology and the Division of Allergy and Immunology.

The number of people – particularly women – who are affected is significant: the National Osteoporosis Foundation (NOF) says some 10 million Americans – 80 percent of those female – are estimated to have osteoporosis, while another 34 million are considered at increased risk for developing the disease due to low bone mass.

Many people still think of osteoporosis as a benign condition that is an inevitable result of getting older. But statistics show that it should instead be viewed as a major health threat that is, in many cases, preventable.

MILLIONS SUFFER DISABILITY AND DEATH

Although osteoporosis can occur at any age, middle-aged females are particularly susceptible because they lose up to 20 percent of their bone mass in the first five to seven years after menopause. This bone density loss has been linked to the estrogen decline that occurs during and after menopause. While pain and loss of mobility often are associated with the condition, statistics published by the NOF show that many patients suffer much more serious outcomes:

- on average, nearly one-fourth of hip fracture patients 50 and over die in the first year after their injury, with mortality for men nearly twice that of women.
- one in five patients who were ambulatory before a hip fracture requires long-term care afterwards, and the same percentage ends up in a nursing home.
- one in two women and one in four

men over 50 will suffer an osteoporosis-related fracture over their lifetime, and women who have one hip fracture are at greater risk of having a second one.

Besides the human toll the bone disease takes, the NOF estimated the cost of care for osteoporosis-related fractures in 2002 at \$18 billion annually and rising.

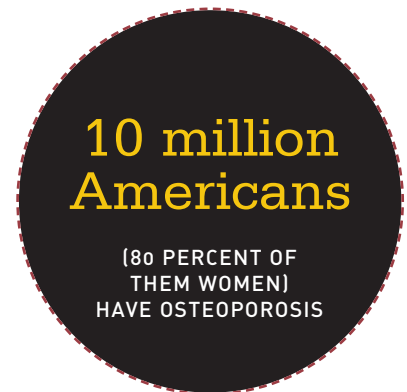
“It is a huge expense to look at the outcome we are trying to prevent, not to mention the mortality,” says Tanner. A hip replacement can cost up to \$75,000, he explains, an amount that dwarfs the cost of preventive medication that might help prevent a hip fracture from occurring in the first place.

RESEARCH BRINGS TREATMENT ALTERNATIVES

Tanner says that perhaps 80 percent of bone health may be linked to the genes we’re born with, while the remaining 20 percent is influenced by lifestyle and other factors. Certain diseases and medications – steroids are one example – can cause bone loss in people of all ages. Taking hormone replacement after menopause and calcium with vitamin D – which aids in absorption – were the earliest treatments, but the drawbacks of both have been revealed by research studies over the years, while other medicines have been developed.

“Calcium plus D are not truly a treatment in and of themselves,” explains Tanner, although taking the supplements regularly has been linked to slower bone loss and, perhaps, fewer hip fractures. Bones need an adequate supply of calcium to remain healthy, but taking the supplement doesn’t actually fix porous bone, Tanner explains.

And even though taking hormones for bone health has been shown to reduce fractures, the drugs are no longer recommended as a treatment since the large, randomized Women’s Health Initiative study linked them to a higher risk of breast cancer, heart attack and other threatening conditions in post-menopausal women.



The first drug approved in the United States specifically to treat osteoporosis, a bisphosphonate branded as Fosamax, was approved by the Food and Drug Administration in 1995. Other types of bisphosphonates now include the brands Actonel, once-a-month Boniva, and the once-a-year medication Reclast. These drugs are called anti-resorptives because they work by slowing or stopping the process of bone breakdown.

“You remodel about 10 percent of your skeleton each year,” explains Tanner, adding that people who do more weight-bearing exercise can remodel more. This lifelong process belies the idea of bone as a fixed organ; instead it goes through a constant process of breaking down and building back cells.

Other drugs that work similarly to the bisphosphonates are calcitonin and estrogen, which now are recommended to treat osteoporosis only in severe cases and if no other options are available.

Raloxifene – Evista is one – is a selective estrogen receptor modulator (SERM) that has the added benefit of reducing low-density lipoprotein cholesterol as well as improving bone density.

And in 2002, the FDA approved the first osteoporosis treatment that actually stimulates new bone formation, a type of parathyroid hormone (PTH) called teriparatide, sold under the brand name Forteo.

“It’s expensive and has to be taken by injection,” observes Mundy. “However, it works very well in people with severe bone loss.”

All of these treatments have specific prescribing targets and carry with them the risk of a number of side effects, so patients should discuss the pros and cons of taking any of them with their doctor.

FUTURE HELP FROM A FAMILIAR MEDICINE?

An internationally renowned investigator in bone biology, Mundy is studying the use of statins – now widely prescribed in pill form to lower cholesterol – to speed the healing of tibia fractures, with an eye toward drawing additional funding for doing further research on using the familiar drug for broader bone health.

“We know that statins work well if they reach the bone,” Mundy explains. In the pill form commonly taken to lower cholesterol, little of the medication gets beyond the liver to reach the bone.

Topical application to the skin seems to overcome that problem, Mundy says, as does injection locally at a fracture site, the delivery approach which will be used in his research study with lovastatin.

Other new drugs being studied are aimed at blocking the breakdown of bone and building bone back.

“The big need in osteoporosis is for a treatment that will restore bone that has been lost,” says Mundy, who is a professor of Medicine in the Division of Clinical Pharmacology and also holds appointments in Pharmacology, Orthopaedics and Cancer Biology. That action would better the effect of most current medications, which generally maintain the bone the way it is.

As the outsized baby-boom generation ages, osteoporosis promises to become a bigger problem in the populace, a trend that already is reflected in the busy schedule of the Vanderbilt Osteoporosis Clinic, Tanner says. He would like to expand the clinic from the current two days a week to five to meet the anticipated demand.

Tanner says one concern in the field is the push at the federal level to cut the reimbursement for the low-radiation dual-energy X-ray absorptiometry (DXA) scans that



S. Bobo Tanner, M.D., left, and Gregory Mundy, M.D.

have been the gold standard for diagnosing osteoporosis and evaluating the benefits of various treatments. Some physician specialists are suggesting replacing the quick procedure that measures bone mineral density – which costs about \$125 – with a CT scan that is four to five times more expensive and exposes the patient to much more radiation, Tanner says.

“It’s a bargain in comparison,” he says of the DXA test. Tanner fears testing for osteoporosis might decline if this effort succeeds, since many patients will resist traveling to a major medical center to get a CT scan and paying more when DXA scans often are available in the doctor’s office.

“Access to this test is going to disappear,” he says. “We have to keep access to bone density measurement available.”

In the future, Tanner thinks new imaging techniques may produce virtual bone biopsies that will foster a better understanding of the bone structure and the limitations and effects of current medications, which could enable more individualization of care.

“We may be able to target which medications are better for which people,” he explains. **VM**

Tips for Maintaining Bone Health

Although women reach their peak bone mass by about the age of 30, they can help maintain bone health by following these lifestyle and health care tips adapted from the National Osteoporosis Foundation.

- get the recommended daily amounts of calcium and vitamin D – which aids in calcium absorption – preferably through food, but otherwise with supplements; adults 50 and older need 1,200 mg of calcium and 800 to 1,000 IU of vitamin D each day.
- to promote the bone remodeling process do regular weight-bearing exercise, which could include walking, weight-training, dancing, jogging, stair-climbing, racquet sports or hiking.
- avoid drinking excess alcohol and smoking.
- talk to your health care provider regularly about your bone health.

The isolation of urinary
incontinence

WRITTEN BY **NANCY HUMPHREY**
ILLUSTRATION BY **DIANA DUREN**

Urinary incontinence ruled Missy Smith's life for more than 40 years.

A car trip meant knowing where the nearest bathroom would be. If she were on the back roads, she'd have gas stations with the cleanest bathrooms in mind. On the interstate she became familiar with how far apart the exits were, and she only shopped at stores with bathrooms.

Smith, 63, of Winchester, Tenn., is one of millions of adults in the United States who experience urinary incontinence, the involuntary leakage of urine. A condition experienced by women twice as often as men, it's embarrassing, frustrating and debilitating, causing some women to result to a reclusive life. Smith, a self-proclaimed "doer and someone who is young at heart," didn't let it stop her active life, but her condition most definitely had the upper hand.

Smith suffered from stress incontinence, the more common of the two main types of incontinence. It causes the leakage of urine when a woman coughs, laughs or sneezes, and is a result of the weakening of the support structures of the urethra and bladder.

Another form is urge incontinence where a woman has a sudden strong urge to urinate and leaks before she can get to the bathroom. It's sometimes called "overactive bladder." Urge incontinence usually gets worse with age, and is often caused by nerve damage that results from certain diseases or surgeries. Some women can have a mixture of both.

Smith, who weighed 87 pounds as a teenager, gave birth to an 8 ½ pound baby at 17. She developed the problem in her early 20s and lived with the condition 24 hours a day. She wore pads all day every day and based her choice of clothing on what would best hide the fact that she was wearing bulky pads. She could leak urine when she coughed,

laughed or sneezed, but also when she stood or sat – basically any time during any activity, including sexual intercourse.

"The worst part for me was living with the threat of always being embarrassed, that there could be an accident at any time," she said. After an unsuccessful attempt to fix her problem in her 40s (urethral plication), she continued to live her life with the condition, figuring she had no choice.

But once she hit 60, she had had enough. "I got to the point where I said 'to hell with this. I can't put up with this any more for whatever time I have left,'" she said. In early 2007, her local gynecologist referred her to Vanderbilt's Daniel Biller, M.D., a urogynecologist who performed a minimally invasive transobturator suburethral sling which has eliminated her incontinence.

Suffering in silence

Having some type of urinary incontinence is common, a normal part of aging, and there are usually two peaks of occurrence— at childbirth (transient incontinence related to the birth process) and either before or after menopause.

But it doesn't mean women who have severe cases have to live with it, Biller says. Many women struggle with it until their mid to latter years before finally having it fixed, he said.

It wakes them up at night, limits their time away from home or from the nearest bathroom, forces them to wear bulky pads or adult diapers, and causes skin irritation and sometimes infections. The National Association for Continence estimates that about 25 million adults in the United States experience urinary incontinence. Despite its prevalence, many women are reluctant to talk to their physician about

it or to seek treatment. A 2001 survey of U.S. adults, sponsored by the NAFC, indicated that only one-fourth of those who had symptoms discussed them with a doctor. A 2004 survey showed the women who do seek care do so after living with their symptoms for more than six years.

It's not known exactly what causes incontinence, but several factors are believed to predispose women to the condition, including genetics and those who have multiple vaginal deliveries resulting in the stretching of the nerves as well as weakness of the pelvic floor musculature. Menopause is also a risk factor because of lack of estrogen, which maintains blood flow to the vagina as well as to the urethra. When a woman loses the engorgement of blood flow from lack of estrogen, she loses some urethral function.

Prior pelvic surgery, particularly hysterectomy, and other factors such as lifestyle issues like smoking might also contribute to the onset of urinary incontinence, said Harriette Scarpero, M.D., assistant professor of Urologic Surgery.

"Many put off coming in to see someone about this problem for many years, in some cases," she said. "They can live in isolation a lot of times, thinking they are the only person with this problem, when in fact it's a very prevalent problem in the post-menopausal population. Women often can't predict when they are going to leak, and when they do, it can be quite profound. We're not talking about just a few drops or wetting a pad, it can be a full out flood in many women, something that can't be contained with any of the barrier methods that exist."

Often women put off addressing their problem because they can't afford to take time away from their other duties – caring for children, a spouse, grandchildren, parents. In many cases they are taking care of multiple generations. "Women have a lot on their plate," Scarpero said.

Can it be fixed?

At Vanderbilt, urologists and urogynecologists both see women with

incontinence. The two specialties work closely together, even sharing a fellowship.

Before any type of treatment is selected, women must first undergo an extensive evaluation process called urodynamics – an evaluation of bladder function, including storage, emptying and urethral function. As part of the consultation process, women take home a voiding diary for homework.

Sometimes incontinence is related to other pelvic floor dysfunction, such as pelvic floor prolapse, or to a patient’s neurologic problems. It’s because of the varied causes of incontinence that urologists and urogynecologists at Vanderbilt work together, sometimes performing different procedures on the same patient.

The three major types of incontinence are treated in different ways. Urge incontinence is treated by anticholinergic medications of the “gotta go” variety seen on TV – such as Ditropan and Detrol – and behavioral therapy like Kegel exercises (contracting and relaxing the pelvic floor muscles) to strengthen the muscles below the bladder, Biller says. The drugs work by decreasing urgency and frequency and urge incontinence by blocking the nerve impulses to the bladder that cause it to contract and leak. But there are side effects, including dry mouth, constipation, headache and blurred vision.

Depending on the findings on the urodynamics testing, women with stress incontinence are encouraged to try Kegel exercises first. Biofeedback or pelvic floor muscle training also may be attempted

before the patient and her doctor consider surgical therapies for those not successful with conservative attempts.

Biller recommends that patients try the conservative route first, and also try avoiding caffeine (a diuretic) and overfilling their bladder by drinking a normal amount of fluid each day – six to eight glasses a day.

“Studies show that menopausal patients who rigorously adhere to bladder retraining, timed voiding and Kegels, improve their symptomatology about 60 to 65 percent. That’s absolutely remarkable,” Biller says.

But if surgery is necessary, the common way to repair stress incontinence is to stabilize the urethra so that with coughing, sneezing and laughing, it is able to maintain its higher pressure or functionality, Scarpero says.

Over the past 20 years, tremendous progress has been made in the development of minimally invasive surgical procedures with faster recovery time, and fewer complications. One of the first procedures to repair stress incontinence was the Burch urethropexy, a more invasive procedure originated by Vanderbilt’s John C. Burch, M.D., MD’23.

Surgeries today are called sling procedures. A sling is formed by taking a piece of the abdominal tissue (fascia) or synthetic material. The man-made sling pushes on the urethral sphincter, thus preventing leakage of urine during stressful movements. These procedures require a small cut in the abdomen and vagina. The procedure can be performed in one of two ways: just above the vagina on the lower abdomen (retropubic) or into the groin creases (transobturator technique). Many different types of the sling procedure have been developed, including a transvaginal tape procedure which uses smaller cuts and can be done as an outpatient surgery.

“In most cases, surgeons choose a sling or two they are comfortable with, and use them all the time,” Biller said. “We are on the forefront of performing

these sling procedures, and we tailor our treatment plans to the patient based on her individual goals and urodynamics findings,” Biller said. “We can offer the least invasive procedure with the fewest complications, and the quickest recovery time to our patients.

Success rates are high, but no patient can ever be 100 percent guaranteed there will be improvement or a cure. And the word “cure” can mean different things to different patients, Scarpero said.

“Is cure zero leakage by pad tests or is cure when the patient tells you she is dry? The two may be very different, therefore many argue it’s only a perception of the patient’s level of cure that’s important,” she said, adding that a patient may be cured of one type of incontinence only to develop another.

“It gets very complicated when you try to fully determine what is cure, so it’s important to counsel patients about success rates and percentages,” Scarpero said. When you look at the literature, the success rates at one year are very high with mid-urethral slings and pubovaginal slings – 90 to 95 percent – but if you look at longer term data, at five years, it drops to about 75 to 85 percent. So it may not be 100 percent, but the success rates are good and durable.”

Smith said she was skeptical about the success of her procedure because she had had poor results with the prior procedure 20 years ago. “But the medical profession keeps making great strides. This has absolutely changed my life.”

She doesn’t have to plan outings anymore bathroom by bathroom, and recently spent two and one-half hours in the dentist’s chair only having to worry about her teeth.

In the fall, she attended a family reunion at the beach in Ocean City, Md. Two years ago, at the last reunion, she wore a bathing suit, but had to head straight to the ocean to get her suit wet – so if she leaked urine it wouldn’t be so noticeable.

This year, she waited awhile. **VM**

**25 million
adults**

NUMBER OF PEOPLE
IN THE U.S. WHO
EXPERIENCE
URINARY
INCONTINENCE

President's Corner

The recently published book, "Onward and Upward," written by our previous Vice Chancellor for Health Affairs, Roscoe R. (Ike) Robinson, M.D., is an interesting story of growth and change at Vanderbilt University Medical Center. This book is also a reminder of the growth and contributions of the Canby Robinson Society (CRS). It is important that all of us at the Medical Center be informed of the tremendous impact of the CRS on this institution.

The CRS was founded in 1978 with a goal to honor and encourage those who contribute to furthering education, research, and patient care at VUMC. In 1979, one year after creation, our membership was 113, and this has increased steadily, to a current membership of more than 2,600.

As membership has increased, there also has been a steady growth in contributions by CRS members. Contributors have unlimited options for giving which support patient care, research and teaching.

Unrestricted gifts to the School of Medicine are used to support financial aid to students while restricted gifts represent the choice of the donor. During fiscal year 2007, total membership contributions totaled just over \$17 million.

Contributions may be cash or documented bequests, and come from members who are current faculty, medical alumni, grateful patients or other friends of Vanderbilt.

In 1992, the CRS made a decision to financially support medical student scholarships that would pay full tuition for three students in each class for a total of 12 students. This commitment has flourished, and in the current academic year, CRS gives full tuition and a cash stipend totaling \$39,600 per year to six first-year students, four second-year students, seven third-year students, and four fourth-year students. Additionally, CRS provides the medical school tuition for 14 M.D./Ph.D. students. These CRS scholarships and other scholarships have played a major part in reducing medical student debt at the time of graduation. For those students graduating from Vanderbilt in 2006, the average debt was \$117,300,

while the national average for private medical schools was \$149,500. CRS is doing well and will continue to do even better. I have appreciated the opportunity to serve as president these last two years, and I look forward to the coming leadership of our president-elect, Kitty Murfree, who will assume office in January.



Lonnie Burnett
President
Canby Robinson Society
VUMC

For more information about the Canby Robinson Society, contact Missy Eason, Director of Donor Relations, Vanderbilt University Medical Center, D-8223, Medical Center North, Nashville, Tenn., 37232-2106, (615) 343-8676 or 8677, fax (615) 343-0809, e-mail: missy.eason@vanderbilt.edu; www.mc.vanderbilt.edu/crs/

Hall's firsthand experience blends with love of giving

Donna Hall and her husband, John, are very familiar with Vanderbilt.

John Hall, the retired chair and CEO of Kentucky-based Ashland Inc., graduated from Vanderbilt University in 1955. He was co-captain of the 1955 football team and named Academic All American. He has been a member of Vanderbilt's Board of Trust since 1987

Donna and John Hall



and served as chair of the board from 1995-1999.

But the Halls' partnership with Vanderbilt became a bit more personal in 1998 when Donna Hall was diagnosed with breast cancer. They sought medical opinions about her treatment from the top cancer centers around the country. Even though they live in Lexington, Ky., she chose the Vanderbilt-Ingram Cancer Center for her care. "They saved my life," she said. "Receiving excellent care was important, but feeling comfortable at the Cancer Center was a real plus. We decided to have my treatment at Vanderbilt where I could have both."

After a year of treatment at Vanderbilt-Ingram from her oncologist David Johnson, M.D., and her surgeon Dan Beauchamp, M.D., which included chemotherapy and a lumpectomy, followed by more chemotherapy and radiation, Donna Hall's cancer is gone, but she

continues to see both doctors annually.

Her experience has made her want to give back. She has been a member of the Vanderbilt-Ingram Board of Overseers since 2005, and she and her husband have given \$1.5 million to fund the Donna S. Hall Chair in Breast Cancer at Vanderbilt-Ingram. The chair will be used to recruit and retain an exceptional clinical director of the breast cancer program. A surgical oncologist with a national reputation will be targeted as the first recipient of the Hall chair.

"This gift is such a wonderful testament to the powerful relationship that develops between cancer survivors and their medical team," said Jennifer Pietenpol, Ph.D., interim director of Vanderbilt-Ingram. "Donna greatly valued the care that Drs. Beauchamp and Johnson, and their colleagues, provided and was in a position to help enhance our

(continued on page 58)

Canby scholars shine in medical school

From marathon runners to world travelers, this year's incoming class of Canby Robinson Scholars brings a wealth of experience and exuberance to Vanderbilt University School of Medicine.

Chris Estopinal graduated from Nashville's Franklin Road Academy before attending the University of Virginia, where he majored in chemistry and minored in religious studies.

While not studying, he enjoys competing in marathons. He ran this year's Boston Marathon.

Chris chose to come to Vanderbilt after working a summer with Katherine Edwards, M.D., in pediatric infectious diseases. "The CRS scholarship locked it in for me," he said. "To graduate without all the financial burden is a huge plus. I'm interested in primary care and international health, so the scholarship will allow me to pursue these career interests."

After graduating from Vanderbilt with an undergraduate degree in molecular and cellular biology, **Audrey Metz** spent a year working in the Eichman lab on protein crystallography.

"I decided to attend medical school at Vanderbilt because I have really enjoyed living in Nashville and going to

Vanderbilt," she said.

She is interested in medicine/pediatrics or women's health as a specialty. "I am especially interested in working in low-income areas with preventive care," she said. "The CRS scholarship gives me the freedom of doing this work right away or doing multiple fellowships after school in different areas of expertise."

Eric Rellinger noticed the welcoming environment of VUSM when he was deciding where to attend medical school.

"Vanderbilt had a culture that was distinct from the other medical schools," he said. "The faculty, staff and students went out of their way to make my visit as pleasant as possible."

Rellinger graduated from Wittenberg University in Springfield, Ohio, with a BS in biology and a BA in chemistry in 2007.

He is interested in lab-based research, and VUSM's new curriculum and new anatomy lab were enticing to him. "This demonstrated to me that Vanderbilt was committed to optimizing the experiences of their medical students," he said.

He is considering pediatric surgery or pediatrics. "Being awarded a CRS scholarship has afforded me considerable flexibility in selecting a career path," he said.

Brian Grieb was introduced to Vanderbilt through the Summer Science Academy sponsored by the Department of Pharmacology.

help women in the future."

Hall said her husband planned the gift in her honor. "I was really touched. I had no idea he was planning to do it. When I found out, I wanted both names on the chair, but he said 'no, you are the one who has gone through the treatment experience. It should be your name,'" she said. "But the names aren't really important. What's important is giving this gift to help in research and treatment and, hopefully, to eventually find a cure."

Hall said she values her time on the Cancer Center board, and is especially excited about Vanderbilt-Ingram's \$10



TOMMY LAWSON

Canby Robinson Society scholars, left to right, are: (front row) Carmen Wolfe, Dana Harrar, Audrey Herrin Metz and Katie Fluke Shaw; and (back row) John Erickson, Eric Rellinger, Chris Estopinal and Brian Grieb.

He participated in the academy in 2006 during his undergraduate studies at Centre College in Danville, Ky., where he earned a BS in biochemistry and molecular biology in 2007.

During that summer at Vanderbilt, he was invited to attend the Medical Scientist Training Program (MSTP) retreat. "I saw both the breadth and quality of research being conducted by Vanderbilt students," he said.

His goal is to become a physician-scientist and examine signal transduction pathways that contribute to cancer progression. "I am honored by the generous gifts of others and their willingness to invest in my future," he said.

Kate Shaw graduated from Georgia Tech with a BS in biology in 2007 before deciding to attend VUSM. While at

million capital campaign to fund expansion of the Henry-Joyce Cancer Clinic. Construction has already begun to improve research areas and dramatically expand the clinic, providing a more comfortable, healing environment for patients and their families.

"We really need this additional space," she said. "We've run out of room, and we need better treatment areas and waiting room space. It's such a stressful time (having cancer), and I have experience from two very different sides – as a board member and also as a patient."

– NANCY HUMPHREY

(continued from page 57)

breast cancer program and extend that care to even more women. Donna and John's generosity and leadership will have a great impact for breast cancer patients now and in the years to come."

Donna Hall said she is impressed with the care she and others receive at Vanderbilt-Ingram. "I received such wonderful treatment there. Everyone is treated equally, in a professional way, but with dignity and respect. It was remarkable to see that happening, and it made us want to give back to the Cancer Center. I hope the gift we are giving will

Georgia Tech, she was involved in outreach organizations, served as creator and chair of the AIDS Awareness Week, and traveled to the Gulf Coast three times with fellow students for reconstruction projects.

"Vanderbilt was my favorite medical school after coming to Nashville for the interview," she said. "The collegial atmosphere and the people who I met during that short visit put Vanderbilt at the top of my list."

She is interested in pediatrics and internal medicine in underserved populations.

"The CRS scholarship will give me the opportunity to interact with and learn from a variety of amazing fellow CRS scholars," she said.

John Erickson also participated in the MSTP while an undergraduate at Case Western Reserve University.

A 2007 graduate with a BS in biology, he is interested in infectious diseases and immunology. "As a physician-scientist my goal is to bridge the gap between laboratory science and clinical applications," he said.

Erickson chose Vanderbilt due to the community and collegiality between students, faculty and researchers. "It also seemed to me that the students worked hard, but they also knew how to relax and have fun when they could," he said. "I think this has a lot to do with the emphasis the deans place on wellness -- both the personal accountability we have for our own wellness and the things the faculty can do to promote it."

Erickson said the CRS scholarship

The Canby Robinson Society's summer outreach tour was led by Donna Glassford, Vanderbilt University Medical Center's Director of Cultural Enrichment.



will ease a lot of the financial burden. "I think that it will increase my quality of life and allow me to do more things that I would otherwise not do because of financial restraints."

The welcoming and nurturing environment at Vanderbilt also attracted **Dana Harrar, Ph.D.**

Harrar earned her BA in biology from Johns Hopkins University before graduating from Harvard University with a Ph.D. in neuroscience in 2007. While at Johns Hopkins, she was a member of the varsity women's swim team. At Harvard she was a medical advocate and rape crisis counselor.

She is interested in women's health, international health and psychiatry.

"The CRS scholarship enabled me to come to Vanderbilt for my medical education, and will enable me to pursue my goal of working with underserved women in both the United States and the developing world," she said.

Carmen Wolfe took a year after receiving a BA in East Asian Studies and Biological Sciences at Vanderbilt University to study acupuncture/moxibustion at Beijing University, earning a Graduate Certificate in Traditional Chinese Medicine in June (*see related article on this page*).

She is also involved in Manna Project International, an organization established by former Vanderbilt graduates to connect college students with service opportunities in the developing world.

After medical school she plans to work in developing nations, either serving as a physician or as an educator of local health care providers.

"The CRS scholarship will provide me with considerable financial flexibility in occupational choice, giving me the freedom to serve in underdeveloped areas without the prohibitive repayment requirements of school loans," she said.

- JON COOMER

Wolfe brings Eastern perspective to VUSM

Carmen Wolfe has traveled the world, exploring many paths that will ultimately shape her career as a physician.

Her experiences have ranged from shamanistic healing rituals to women's sewing circles in India where foreign nurses offered advice to local women on female health.

"I was fortunate to have many unique health-related opportunities in Central America, India, Tibet and China," the new Canby Robinson Society scholar said.

As part of her deferred year from VUSM, she moved to Beijing, China, in May 2006 where she studied traditional Chinese medicine, including acupuncture/moxibustion, and gained a unique perspective on health and the human body.

"Their medical system (Eastern medicine) is based on a philosophy, a way to explain the mind-body connection," she said. "It was a year unlike any other."

She earned a graduate certificate in Traditional Chinese Medicine in June from Beijing University, and now that she is a VUSM student, she wants to promote understanding and mutual respect between Eastern and Western medicine to ultimately benefit patients.

"The most important thing is to have an open dialogue to benefit the patient," she said. "If doctors knew more about acupuncture, maybe they would be more willing to refer patients. Wolfe points to the great work being done at VUMC's Center for Integrative Health, but thinks more patients could benefit from Eastern and other non-traditional forms of medicine.

Her travels have piqued her interest in studying other cultures to advance her medical career and personal life. She is currently considering the possibility of

(continued on page 60)

WHERE ARE THEY NOW? JOSEPH AGOSTINI, M.D.

When Joseph Agostini, M.D., graduated from Vanderbilt University School of Medicine in 1997 he moved back home to Connecticut for an internal residency at Yale-New Haven Hospital, taking with him many fond memories of his time at Vanderbilt.

Now on faculty at Yale University School of Medicine as assistant professor of Medicine, Agostini encourages trainees to consider Vanderbilt.

“My experience was outstanding, and I like to make sure the trainees I encounter here in Connecticut realize the opportunities available at Vanderbilt,” he said.

In addition to his faculty position, Agostini sees patients at an outpatient geriatrics assessment center, serves as an attending on the inpatient medicine/geriatrics teaching services, and has an office in the Clinical Epidemiology Research Center at VA Connecticut. About three-fourths of his time is spent on research related to medication prescribing in older adults, addressing issues of the risks/benefits of multiple medication use in aging seniors and efforts to improve the quality of drug prescribing.

Ultimately, he hopes to develop strategies to help clinicians and patients who take multiple medications maximize the safety of their medication regimens and minimize drug-related

adverse effects.

Agostini credits the Canby Robinson Scholarship program with allowing him to pursue academic research.

“I felt and continue to feel immensely fortunate for the honor,” he said of the scholarship. “The decision to pursue an academic career in geriatrics was made much easier by having had the CRS award.”

Agostini lives with his partner just outside of New Haven. He enjoys book collecting in his spare time, collecting Sherlock Holmes-related material and also Christopher Morley first editions. His most recent find is much more occupationally related--a first edition copy of probably the first book in English on geriatrics, published in London in 1724.

- JON COOMER

Joseph Agostini, M.D., by the gardens of Versailles, France



(continued from page 59)

completing a Medical School Emphasis project through the Institute of Global Health, which could take her anywhere from Mozambique to Ecuador.

During her undergraduate studies at Vanderbilt, she was involved in Manna Project International (MPI), an organization established by former Vanderbilt graduates to connect college students with service opportunities in the developing world.

During college she participated in local service opportunities, organized a spring break service trip to El Salvador, and served as MPI treasurer during her senior year. She also helped raise nearly \$15,000 for a new medical clinic in Nicaragua.

After months of traveling across the nation visiting medical schools, Wolfe realized that Vanderbilt was her best option for medical education.

“With an innovative new curriculum, Vanderbilt offered an amazing combination of traditional lecture-style education with the ability to personalize your experience through the preceptorship and Emphasis programs,” she said. “The faculty and administration at Vanderbilt truly care about their students, and work hard to ensure that our educational experiences motivate us to study well and become considerate, compassionate and competent physicians.”

After graduation she would like to continue work and do research abroad, and is considering a second degree in public health.

She is currently a diabetes educator at the Shade Tree Clinic, a student-run free health care clinic in East Nashville, where she works one-on-one with patients newly diagnosed with diabetes.

- JON COOMER

Steven Gabbe, M.D., dean of VUSM, met with (left to right) Caroline Webb, James Webb and Jud Randolph, M.D., as they signed a gift agreement for the Caroline Bartlett Webb Family and Judson G. Randolph Family Scholarship.



save this date
CRS Dinner
May 17, 2008

ANN H. PRICE, M.D.
Executive Director
for Medical Alumni Affairs



CONTACT

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VMAA ProQuest Database Trial

Through collaboration with the Eskind Biomedical Library, Vanderbilt Medical Alumni Affairs launched the Eskind Biomedical Digital Library Project (EBDLP, Web site: http://www.mc.vanderbilt.edu/alum_diglib/) three years ago. While feedback from our medical alumni has been positive, many, who no longer have a VUID and password to access Eskind Biomedical Library's main digital library, continue to ask for greater full text online journal availability. In researching how sister institutions serve their medical alumni, the ProQuest Database surfaced as a potential option for offering more online journal access.

After a review of ProQuest's digital resources (approximately 400 online journals), the VMAA Board elected to contract with ProQuest for a 12-month trial to evaluate its value for our VMAA membership. (Trial is limited to 500 medical alumni.)

If you have not enrolled, we still have some participant slots available.

VMAA Trial participants should be:

- Vanderbilt Medical Alumni interested in accessing online medical journals
- Important Note: Alumni with current access to an academic subscription (such as Vanderbilt faculty and faculty at other academic institutions) already have access to a much richer

online journal database than that provided by ProQuest, but may still participate in this trial if interested.

Trial participants will receive:

- Free access to the ProQuest Digital Journal Database of more than 400 journals
- An opportunity to assess the potential utility of ProQuest as a general VMAA benefit

Trial participants will be expected to:

- Answer a brief questionnaire at the beginning of the trial and then at three-month intervals.

If you are interested in participating in this trial, please contact me at ann.price@vanderbilt.edu. I hope you will consider helping the VMAA evaluate the utility of this service.

New Parking Hang Tags

New bar-coded hang tags are now in use for our Middle Tennessee-area Vanderbilt Medical Alumni utilizing VMAA's free parking option in the South Garage. If you have not received your new bar-coded hang tag, or if you want to learn more about VMAA's free medical alumni parking privilege please contact Lisa Gusty at: lisa.gusty@vanderbilt.edu or (615) 322-6146.

E-mail Address Updates

E-mail is the preferred mode for rapid communication with our Vanderbilt medical alumni. Please keep the VMAA posted with your e-mail address updates. Send these to: medalum@vanderbilt.edu. If you have two or more e-mail addresses you use on a routine basis, please indicate the preferred one for receiving VMAA communications.

Reunion 2008

Preparations are in full swing for our next Vanderbilt Medical Alumni Reunion, Oct. 23-25, 2008. All medical alumni are invited to attend, but special anniversary class celebrants are especially encouraged to return to campus.

5th	10th	15th	20th	25th	30th	35th	40th	45th	50th	Quinq Plus
2002	1997	1992	1987	1982	1977	1972	1967	1962	1958	1957 and earlier
2003	1998	1993	1988	1983	1978	1973	1968	1963	1959	

Please visit our Web site at www.mc.vanderbilt.edu/medschool/alumni to stay posted on Reunion 2008 news.

KEY

- MD - Medical School Graduate
- HS - House staff
- FE - Fellow
- FA - Faculty
- CF - Clinical Faculty

* Indicates CRS member

40s

Otis Gene Austin, M.D., MD'43, celebrated his 90th birthday recently at his home with his wife, Betty, in Fort Myers, Fla. He practiced medicine in Medina, Ohio – mostly ob/gyn – from 1950 until 1987.

Herbert L. Glass, M.D., MD'49, HS'51-'52, has been spending January-March for the past five years as a volunteer at two children's medical facilities in San

Miguel de Allende, Mexico. His wife, Helene, (VU'48) is a member of the American Watercolor Society and is represented by an art gallery in San Miguel de Allende.

***Alvin F. Goldfarb, M.D.,** MD'47, is now Emeritus Professor of Obstetrics and Gynecology at Jefferson Medical College of Thomas Jefferson University Hospital. He is the executive director of the Adolescent Wellness Achieved Through Resources in Education Foundation (the AWARE Foundation) and also writes columns for nurse practitioner communications. Goldfarb and his wife, Arlyne, celebrated their 59th wedding anniversary on Sept. 19, 2007. Four of their children are married, and they have five grandchildren. Their eldest lives in London and has been there for 25

years, working for National Public Radio and the BBC, and working on his second book.

James R. Hamilton, M.D., MD'46, retired from the Department of Dermatology at Vanderbilt in December 2004. He lost Ruth, his wife of 60 years, recently. Hamilton, who has two sons – Jim Jr., and John -- recently moved to a retirement community in Brentwood, Tenn.

G. B. Hodge, M.D., MD'42, of Spartanburg, S.C., was listed in the 2008 edition of "Who's Who in America" and in the 2008-2009 edition of "Who's Who in Science and Engineering." His son, Byron Hodge, M.D., is a urologist/ oncologist in Lakeland, Fla.; son, John, has a law degree; and daughter, Susan, has an MBA degree from Duke.

ogy-oncology practice in 1994 and is enjoying retirement "immensely."

Donald B. McCormick, Ph.D., Ph.D.'58, is being honored by Emory University with the annual McCormick Seminar, named for the former chairman of the Department of Biochemistry and Executive Associate Dean for Sciences in the School of Medicine. The graduate program in Nutrition and Health Sciences at Emory is honoring McCormick by bestowing the "McCormick Award" on the graduate with the highest research achievement each year.

William Gardner Rhea, Jr., M.D., MD'58, HS'58-'64, is working part-time at East Tennessee State University Medical School as a clinical professor of Surgery. His oldest son, W.G. Rhea III, is a U.S. Navy commander in Norfolk, Va.

correction

Editor's note:

In the last edition of Vanderbilt Medicine, we mistakenly put an honor for Ben V. Branscomb, M.D., MD'47, HS'48, in the "in memoriam" section of the magazine. Branscomb, of Birmingham, Ala., is a nationally renowned researcher and pioneer in pulmonary medicine whose career has spanned six decades. In 2006 he received the Lifetime Achievement Award in the Birmingham Business Journal's Health Care Heroes program.

Dr. Branscomb kindly pointed out the unfortunate placement of the news of his award, and sent this note.

July 23, 2007

Dear Madams/Sirs,

At 6 a.m. today, after I got out of the hot tub in our greenhouse, I repaired to my workshop where I reconstructed an easel for my wife Jane's studio. While eating a BLT sandwich, I cooked up a salsa verde using ingredients from our garden. Our cardiologist daughter Betsy (BA '74) and her husband, Dr. George Joe (BA '73) then challenged me to draw the brachial plexus. At 5 p.m. we will attend an opening at the Birmingham Museum of Art. At 6 we will have dinner at the Mountain Brook Club with friends including two distinguished Vanderbilt medical alumni, Dr. Wood Herren and Dr. Robert Yoe. The most difficult decision I have confronted all day has been whether to cut that BLT on the square or diagonally from corner to corner.

My copy of the excellent *Vanderbilt Medicine* arrived today. Based on the above I would submit that the report of my demise on page 58 was erroneous.

Sincerely,
Ben Branscomb, M.D.

50s

***Paul H. Barnett, M.D.,** MD'58, retired from VUMC two years ago, and is volunteering one day a week at the Faith Family Clinic in Nashville, serving the local indigent population, working part-time for the Saint Thomas radiation oncology group, and one day a week with Vanderbilt second-year students in the physical diagnosis course. He holds season tickets for Vanderbilt football, basketball and baseball, and reports that his guitar and piano teacher recently asked if he had any interest in art.

***Joe Cromeans, M.D.,** MD'53, of Scottsboro, Ala., retired in April 2006 but still is administrator of the 52-year-old Cromeans Clinic PC in Huntsville, Ala., which has about 130,000 patient records, Cromeans says. When he's not receiving honors – he was named Doctor of the Year three years in a row – he has been busy bringing retail into Scottsboro. He manages Jackson Square Shopping Center and other rental properties.

***Guy T. Gillespie Jr., M.D.,** MD'52, retired from his hemato-

60s

John Christensen, M.D., MD'67, retired from private practice in 2005 and is now chief of anesthesia at an outpatient surgery clinic at the University of Southern California.

Richard Dean, M.D., HS'68-'74, FA'75-'87, has retired from Wake Forest University and Wake Forest Baptist Medical Center, where he served as chairman of the Department of Surgery at the School of Medicine, Chief of Surgery at North Carolina Baptist Hospital, senior vice president of Wake Forest, and CEO of Wake Forest University Health Sciences since 1987. During his tenure clinical activities at Wake Forest more than doubled. Research funding grew from \$98 million to \$200 million a year, and the medical school faculty grew from about 700 to more than 900. Dean is also chairman of the board of the Piedmont Triad Research Park, and of the Winston-Salem Chamber of Commerce and is active in the community. The Old Hickory Council of the Boy Scouts awarded him the Distinguished Citizen Award in 2005.

***Warren McPherson, M.D.,** HS'66-'72, was recently named Medical Director for the Middle Tennessee Reserve Corps. He spent 30 years in the clinical practice of Neurosurgery and was chairman of the State Volunteer Mutual Insurance Company for 11 years, until 2005. He has been a board member for nine years with Physicians Insurance Association of America and served as its chairman for four years. In 2001, he received the National "Physician Executive Award" from the American College of Medical Practice Executives. Previously chief of staff at Middle Tennessee Medical Center, he is incoming president of the Vanderbilt Medical Alumni Association and is a marketing consultant for LifeWings.

***John B. Neeld Jr., MD.,** MD'66, HS'66-'67, was elected chair of the American Medical Political Action Committee in December 2006. In March 2007 he was awarded the John McCoy Physician Leadership Award at Northside Hospital in Atlanta, and in May 2007, received the "Excellence in Government Award" from the American Society of Anesthesiologists.

Larry H. Parrott, M.D., HS'60-'62, has retired and is a volunteer teacher at Medical University of South Carolina and clinical professor of Pathology at the University of South Carolina. He also works with the Community Medical Clinic in Camden, S.C. The grandfather of five still enjoys golf and horseback riding.

J. Michael Reinhart, M.D., MD'67, HS'67-'68, retired in November 2005, but he's still busy. He has a volunteer job singing for Alzheimer's patients, swims laps and enjoys Pilates.

Charles Sachatello, M.D., HS'61-'67, received a patent on a needle holder that cuts sutures in addition to being a standard needle holder. The first produced is a disposable needle holder for emergency room use, and he is

currently designing one for routine OR use. He is recovering nicely from a liver transplant in January 2006 due to liver disease of unknown cause. In August 2007 he was appointed to the Board of Trustees by Kentucky Gov. Ernie Fletcher.

Louis Underwood, M.D., MD'61, HS'61-'65, has moved to Rockville, Md., to be with family. He also has a Web site, www.endocon.com, that houses a newsletter he does for endocrinologists all over the world.

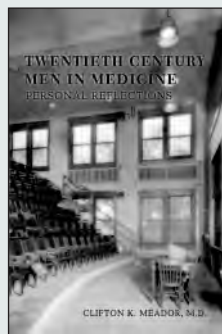
70s

***Susan Andrews, M.D.,** MD'78, and her Murfreesboro practice were included in a recent *Annals of Family Medicine* article (vol.5.no.3, May/June 2007) entitled "Different Paths to High-Quality Care: Three Archetypes of Top-Performing Practice Sites." The practice was identified as one of the "Technofiles Archetype" model practices. Of note, Andrews' practice was previously selected to participate in the AAFP's TransforMED national demonstration project, an effort designed to study a new practice model for primary care with the goal of moving practices to "practices of the future" with highly patient-centered, evidenced based, quality oriented health care utilizing electronic health records and Internet access for patients.

Michael Brenner, M.D., MD'75, HS'75-'80, Theodore B. Bayles Professor of Medicine at Harvard Medical School and chief of the Division of Rheumatology, Immunology and Allergy at Brigham and Women's Hospital in Boston, has been elected to fellowship in the American Academy of Microbiology. Brenner joins about 2,500 fellows, elected annually through a highly selective, peer-reviewed process, based on their records of scientific achievement and original contributions that have advanced microbiology.

Ronald Bronitsky, M.D., MD'77, HS'77-'80, has stepped down as

book focus



***Clifton K. Meador, M.D.,** MD'55, HS'59, FE'60, has authored a book, "Twentieth Century Men in Medicine: Personal Reflections." In the years since Meador graduated from Vanderbilt University School of Medicine, he has trained under eight "inspired" teachers. Each chapter of the book, published by iUniverse, Inc., is devoted to his personal interactions with each of these eight men – strong leaders in medicine who helped each other through their wisdom and insight. They aren't biographies, but glimpses of each professor's

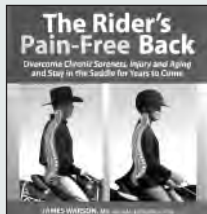
method of teaching and his philosophy of medicine. These stories span the mid 20th century, from 1952 to 1973. During that time, the knowledge of medical sciences expanded enormously, and Meador's stories return to a time in medicine of careful listening to sick people at the bedside.

Verne C. Lanier Jr., M.D., MD'66, HS'66-'71, and **John B. Breinig, M.D.,** MD'66, HS'66-'68, performed several selections together in August 2007 at Scarritt Bennett Center's Wightman Chapel. Lanier played trumpet and flugelhorn and Breinig, the organ.



Royce Dawson, M.D., MD'52, HS'52-'58, left, receives his Quing medal from the ceremony he missed in 2002. Celebrating with him is his wife, **Lucy Buford Dawson, VU'54,** and good friends **Glenn Greene, M.D.,** MD'52, HS'54-'57, and his wife, Virginia.





book focus

***James S. Warson, M.D., MD'66, HS'66-'74,** a neurosurgeon for nearly 25 years, and a specialist in equestrian back injuries, has authored a book, "the Rider's Pain-Free Back." A supple, strong and healthy back is ideal for equestrians, but too many suffer

from back injury, stress or strain, causing pain while in the saddle or the inability to ride at all. In the book, published by Trafalgar Square, Warson takes a look at the human back in easy-to-understand terms, illustrating how various movements in the saddle affect the rider's back. The lifelong horseman then outlines straightforward steps that can be taken to keep the back healthy while riding. The book includes step-by-step instructions and photos for 18 stretches and exercises for a do-it-yourself physical therapy plan for those already dealing with back pain.



This group of medical alumni manage to get together at least once a year. Here, at Perdido Beach, are, left to right, Henry A. Callaway, M.D., MD'54, HS'54-'55, Carl A. Grote Jr., M.D., MD'54, James M. Callaway, M.D., MD'56, HS'60-'64, John W. Boldt, M.D., MD'54, HS'54-'59, Swan B. Burrus, M.D., MD'54, HS'54-'58, and Byron E. Greene Jr., M.D., MD'54, HS'54-'56.



U.S. Rep. Marsha Blackburn (R-Tenn.), left, and Rose Grindstaff, right, president of the American Cancer Society, Nashville-Middle Tennessee, present G. Patrick Maxwell M.D., MD'72, the Congressional Recognition of Merit Award. The celebratory event was hosted by Vanderbilt School of Nursing Dean Colleen Conway-Welch, her husband, Ted, and Rose and Doug Grindstaff.

director of Presbyterian Hospital's Intensive Care Unit in Albuquerque, N.M. His practice now focuses on outpatient management and patients with pulmonary disease. He was recently named in a patient survey as a top-10 doctor in the Presbyterian System. Personally, he's busy, too. He completed a three-mile rough water swim at La Jolla, Calif., and "lived to tell about it," and is a member of the Bosque Bassoon Band and New Mexico Symphony Chorus. This past summer, he performed Beethoven's Ninth Symphony with the Philadelphia Orchestra in Vail, Colo.

***Robert Erickson II, M.D., MD'72, HS'74-'75,** reports that his son, John, was admitted into Vanderbilt's M.D./Ph.D. program this year. He and his wife, Marti, have eight children and one grandchild.

***Arthur Fleischer Jr., M.D., HS'76-'80, FE'80-'81,** received the Distinguished Alumnus Award for Professional Achievement from the Medical College of Georgia in April 2007. In October, he was installed as president of the Society for the Advancement of Women's Imaging in Chicago.

John Grimaldi Jr., M.D., MD'78, and his partner, Mark Barnes, have moved to Memphis, Tenn., from New York City. Grimaldi joined the UT Memphis Medical School psychiatry faculty, and Barnes is now COO of St. Jude Children's Research Hospital.

John Huff, M.D., MD'77, HS'77-'81, FE'81-'82, has returned to Vanderbilt as associate professor in the Department of Radiology and Radiological Sciences, chief of the section of Breast Imaging, and Imaging Director for the Vanderbilt Breast Clinic. He was previously director of breast imaging at Baptist Hospital and the Baptist Hospital Comprehensive Breast Care Center in Nashville for 15 years. His wife, Beth Colvin Huff, M.S.N., is an associate in Obstetrics and Gynecology.

***R. Kirby Primm, M.D., HS'70-'76, FA'79-'84,** of Wenatchee, Wash., has been elected president of the North Pacific Society of Internal Medicine, an organization of internists and internal medicine subspecialists from Washington, Oregon, Idaho and British Columbia.

Peter C. Rawlings, M.D., MD'79, has been practicing pediatrics in Chattanooga for 21 years with Pediatric Diagnostic Associates. He is the current president of the Chattanooga Hamilton County Medical Society and serves on the board of the Children Nutrition Program for Haiti, having gone there for medical missions since 2002. He and his wife, Milly, have three children – Joan, who is in Nashville pursuing a nursing degree; Nate, a graduate of Princeton who is in the U.S. Army, stationed at Fort Hood, and scheduled to go back to Iraq in December 2007; and Lydia, who is getting her master's degree in early childhood education at the University of Tennessee Chattanooga.

***Richard M. Silver, M.D., MD'75,** has been named Distinguished University Professor at the Medical University of South Carolina in Charleston, S.C., the highest academic distinction given by the university. He is director of the Division of Rheumatology and Immunology, a position he has held since 1995, and holds a dual appointment in the Departments of Medicine and Pediatrics. Silver is an internationally recognized expert in the disease of scleroderma, and was recently named "Physician of the Year" by the National Scleroderma Foundation.

80s

Daniel Burch, M.D., M.B.A., MD'84, HS'84-'87, has joined CeNeRx BioPharma as executive vice president of Research and Development and Chief Medical Officer. He will play a critical role in building and advancing

the CeNeRx product portfolio and leading its research and development programs. Burch's industry experience includes 15 years of developing new medicines at Abbott Laboratories, SmithKline Beecham and GlaxoSmithKline. At GSK, he was responsible for building and managing the global neuroscience drug development portfolio and was accountable for delivering important CNS products addressing depression, movement disorders, pain and Alzheimer's disease.

Michael D. Callaway, M.D., MD'83, HS'83-'86, has been named medical director for Heritage Medical Associates in Nashville. His daughter, Becky, married in June 2007 and daughter, Laura, will marry in April. His son, Carter, is a freshman at Montgomery Bell Academy.

Christopher Cates, M.D., HS'82-'85, FE'86-'89, FA'87-'88, is an interventional cardiologist at Emory University School of Medicine and director of Vascular Intervention at Emory University Hospital and Emory Crawford Long Hospital in Atlanta. He served as a planning director of the International Andreas Gruntzig Society's Committee, designed to commemorate the 30th anniversary of the first coronary angioplasty. The observance was held in Zurich, Switzerland in September 2007. The Gruntzig Society has an exclusive membership of only 150 members worldwide.

Erich B. Groos Jr., M.D., MD'87, has completed a two-year term as president of the Tennessee Academy of Ophthalmology. He is medical director of the DCI Middle Tennessee Eye Bank.

N. Lindsay Harris, M.D., MD'88, has changed jobs. After being director of Sports Medicine at the University of Colorado Department of Orthopaedics, he is now fellowship director of the Aspen Foundation for Sports

Medicine, Education and Research.

Lee W. Jordan, M.D., MD'81, is medical director of the Heart Failure Program at Riverside Methodist Hospital in Columbus, Ohio.

James Evans Lyne, M.D., MD'87, began offering a house call service in March 2007 to patients in Knoxville, Tenn., fulfilling a longtime goal of providing personalized, on-the-spot care. He is limiting his house calls to the West Knoxville area, and is trying to limit the calls to regular business hours. Lyne, who also teaches classes in aerospace engineering and biomedical engineering at the University of Tennessee, worked for many years on the emergency room staff at the University of Tennessee Medical Center, at walk-in clinics, and Lakeshore Mental Health Institute.

***Ming Hsu Robinson, M.D., MD'88 HS'88-'92,** of Laguna Hills, Calif., is in a solo ob/gyn practice in Orange County. She and ***William Edward Robinson, M.D., Ph.D., Ph.D.'88, M.D.'92,** have been married for 21 years and report they enjoy living in southern California and watching the Anaheim Ducks hockey team.



A group of 1978 alumni got together at a recent University of Virginia football game. Back row, left to right, Russ Leftwich, M.D., MD'78, HS'78-'81, and Ellen Nygaard; Front row, left to right, Deborah Smith, M.D., MD'78, HS'78-'81, John T. Cobb, M.D. MD'78, and Thomas Nygaard, M.D., MD'78.

Stephen Sobel, M.D., MD'82, was chosen the 2007 Teacher of the Year in Psychiatry by the United States Psychiatric and Mental Health Congress. He is a consulting psychiatrist for the San Diego Chargers football team and for the San Diego Padres baseball team, is a clinical instructor at the University of California at San Diego School of Medicine, and has a private practice of Adult and Adolescent Psychiatry in San Diego. He has been married for 21 years and has a 16-year-old daughter.

***Troy Storey, M.D., MD'87,** HS'87, completed a musculoskeletal radiology fellowship in 2006 and has joined the faculty at the University of Florida College of Medicine as an assistant professor.

Art Wamil, M.D., Ph.D., FE'88-'90, HS'98-'01, serves as head of the Department of CNS (Neurology and Psychiatry) at the U.S. Clinical Research Unit at Sanofi-Aventis U.S. Inc., and medical advisor in Neurology, Psychiatry, Pain and Sleep Medicine and Pediatric Neuropsychiatry in Malvern, Pa.; Bridgewater, N.J., and Paris/Chilly-Mazarin, France. He oversees more than 40 clinical studies, 10,000 patients, and 1,000 investigative sites in the United States.

Jeffrey R. Prinsell, D.M.D., M.D., MD'86, HS'86-'88, has been named to the American Academy of Sleep Medicine's Task Force to update the standards of practice parameters for



volunteer doctors – is part of a broader global effort to combat avoidable blindness.

"It's incredible so many people (in developing countries) have to struggle with it when there are such cost-effective treatments," Van Meter, a University of Kentucky professor and medical director of the Lions Eye Bank of Lexington, told the Courier Journal.

Recruited by a colleague, Van meter first traveled with Orbis in 1986 to Baghdad to perform transplants during the Iran-Iraq War. He has worked in countries including the Sudan, Peru, Haiti, Panama and Romania.

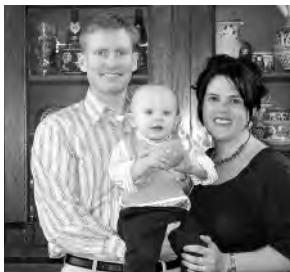
"I returned from a week in Syria exhausted, but with a very good feeling that at least I had done a small part," Van Meter told the newspaper.

worthy of note

Woodford Van Meter, M.D., MD'79, a Lexington ophthalmologist, visited Syria this past summer aboard Orbis International's flying eye hospital as part of a three week mission to restore sight, teach surgical techniques and plant prevention networks. According to a front-page article in Louisville, Ky.'s, Courier Journal, Van Meter's works with Orbis – a non-profit humanitarian organization that over the past 25 years has treated millions of people with help from



Abigail Rose Duncan was born to Coley Bryant Duncan, M.D., FE'03-'07, and his wife, Tara, on July 27, 2007.



Chris Hudson, M.D., MD'98, is shown here with his wife, Christiana, and their son, George Brooks, born in April 2006. Hudson is pursuing a Master's of Public Health at Harvard University. He received a full scholarship as part of the U.S. Air Force's three-year Residency in Aerospace Medicine program.



Kenneth Babe, M.D., MD'91, HS'94, '96, stays busy with three sons – William Penn (called Rives after his maternal great-grandfathers), was born May 9, 2007, and is shown here with Kent, left, and Tom.

obstructive sleep apnea surgery. He was also elected chair of the American Association of Oral and Maxillofacial Surgeons' Clinical Interest Group on Sleep-Related Breathing Disorders, and is current president of the American Board of Dental Sleep Medicine. He lives with his wife and two sons and maintains a private practice of oral and maxillofacial surgery in Marietta, Ga.

***William Edward Robinson Jr., M.D., Ph.D.,** Ph.D.'88, MD'92, is a full professor at the University of California-Irvine, has a joint appointment with the Microbiology department, and mentors graduate students. He is very involved in UCI's M.D./Ph.D. admissions committee and graduate school education. He is married to ***Ming Hsu Robinson, M.D.,** MD'88, HS'88-'92.

90s

Thomas T. Dovan, M.D., HS'97-'00, has joined Elite Sports Medicine and Orthopaedic Center in Nashville, specializing in surgery of the hand, shoulder and upper extremity. Prior to returning to Nashville, he practiced medicine in Georgia.

Pamela J. Fall, M.D., FE'92-'94, associate professor of Nephrology at the Medical College of Georgia's Department

of Medicine, has been elected to membership of two American Society of Hypertension Inc., committees. She serves on the membership committee and co-chairs the Public Policy/Hypertension Specialist Committee of the society's Carolinas and Georgia chapter. She has been on the faculty of the Medical College of Georgia since 1994.

Alexander Fan, M.D., MD'96, associate director of Inpatient Psychiatry Services in the Department of Psychiatry and Behavioral Neurosciences at Cedars-Sinai Medical Center in Los Angeles, has received a NARSAD Young Investigator Award for 2007 to study the therapeutic potential of allopurinol for bipolar mania.

Mark "Tag" Filley, M.D., HS'95-'00, is practicing emergency medicine with Greater Houston Emergency Physicians at Conroe Regional Medical Center. In May 2007, he started a fellowship in Houston, Texas, in Interventional Pain Management and plans on opening his own practice in 2008. He and his wife, Alicia, have three children – Collin and Aidan, both 9, and Alaina, 5 – and were awaiting the birth of another child in December.

***Jeremy H. Freeman, M.D.,** MD'99, is a family physician in his hometown of Blacksburg, Va. He and his wife, Laura, had their third child, Rebecca Claire, on June 1, 2007. She joins big brothers Sam and Luke.

***Joan Collier Henning, M.D.,** MD'97, welcomed a son, James Copeland Henning in June 30, 2007.

Jeffrey Maxwell Holzbeierlein, M.D., HS'94-'00, has been named the John W. Weigel associate professor of Urology at the University of Kansas Medical Center. He is an assistant editor for the *Journal of Urology* and is serving on the executive board for

the Society of Urologic Oncology and the South Central section of the American Urological Association. He and his wife, Jill, have three children, Helen, Max, and Cate, and are expecting their fourth child in May 2008.

Chris Iorio Jr., M.D., MD'98, HS'98-'01, and **Tami Stone Iorio, M.D.,** MD'98, HS'98-'01, welcomed their fourth child, Leo on June 23, 2007. He joins siblings Julia, Colvin and Lukas. Chris was recently named Associate Medical Director of the ICU at Columbus Regional Hospital in Columbus, Ind. He continues to practice Internal Medicine and Critical Care Medicine.

Steven Lilly, M.D., MD'98, is a faculty member in internal general medicine at University of Texas Southwestern in Dallas. He welcomed a second daughter, Abigail, in October 2007.

Allison Messina, M.D., MD'98, is a clinical assistant professor of Pediatrics in the Division of Pediatric Infectious Disease at the University of South Florida, practicing at All Children's Hospital and Tampa General Hospital. She finished her subspecialty training in infectious diseases at UT Southwestern in 2006. She and her husband, Chuck, have two sons, Edward, 3, and Alistair, 7 months.

Marilyn Michaud, M.D., MD'91, HS'91-'94, FE'94-'95, has been named vice-president of the Frist Clinic and medical director of the new Frist Express Clinic in Nashville. She also serves on the board of Tennessee Women in Medicine, and is the mother of 7-year-old twins, Otto and Olivia, and Amelia, 3.

Niki Oquist, M.D., FE'90-'91, has been appointed senior vice president of Medical Affairs for CME LLC, a leading provider of fully accredited continuing medical education programs. He will be responsible for accreditation, managing content development

for all educational offerings and serves as a professional liaison between CME LLC and advisory boards, medical directors and other clinicians. A board certified pediatrician, prior to joining CME LLC he held various management positions with MedImmune Inc.

Seenu Reddy, M.D., M.B.A., HS'95-'02, is professor of Surgery and director of Thoracic Aortic Surgery at the University of Texas Health Science Center at San Antonio, a group with the largest experience with endovascular treatment of thoracic aortic disease in San Antonio.

John O. Schorge, M.D., MD'93, is associate professor of Gynecologic Oncology at University of Texas Southwestern Medical School in Dallas, Texas. He and his wife, Sharon, celebrated their 16th wedding anniversary in the summer of 2007 and have three children: Dante, 5, Lena, 4, and Rocco, 3.

Nathan A. Shapira, M.D., Ph.D., Ph.D.'93, MD'95, has been named Executive Director of Clinical Research and Development and Deputy Chief Medical Officer of Tikvah Therapeutics, Inc., a biopharmaceutical company in Atlanta focused on new treatment options to better manage central nervous system diseases. He will help to lead teams of researchers in the design, development and execution of clinical development programs for Tikvah Therapeutics' neurological and psychiatric pharmaceutical products. He also serves as clinical assistant professor of Psychiatry and Behavioral Sciences at the Emory University School of Medicine, and adjunct assistant professor of Psychiatry at the University of Florida College of Medicine.

Karl A. Sillay, M.D., HS'99-'06, was named Director of



Kent Handfield, M.D., MD'05, married Nicole Summer Twigg in San Diego on Jan. 20, 2007. He is now serving in the U.S. Navy as an Undersea Medical Officer and a primary care physician for submarine sailors in New London, Conn. The couple lives in Mystic, Conn.

Functional Neurosurgery at the University of Wisconsin, Madison, after completing a fellowship at the University of California San Francisco. He and his wife welcomed their first child, Andrew Carl, on May 25, 2007.

Jonathan C. Smith, M.D., MD'98, was inducted as a Fellow of the American College of Surgeons last year and into the New York Head and Neck Society. He is currently a clinical assistant professor and site director for the Weiler Division, Department of Otolaryngology-Head and Neck Surgery at Albert Einstein College of Medicine. He married Kathryn Anolik on June 10, 2007.

Ryan W. Stewart, M.D., MD'98, was voted one of the top doctors in San Diego, Calif., in 2005 and 2006 by San Diego Magazine. He has two sons, 4 and 2, and still enjoys surfing.

2000-

Sean C. Brock, Ph.D., Ph.D.'03, has joined the national intellectual property law firm Woodcock Washburn LLP as an associate. After receiving his Ph.D. at Vanderbilt, he received his law

degree from the University of Tennessee College of Law in 2007.

Matthew Busam, M.D., MD'01, HS'01-'06, has returned home to Elder, Ohio, near Cincinnati, and is now practicing at Cincinnati SportsMedicine and Orthopaedic

Paul DeFlorio, M.D., MD'01, married Amanda Carvell in October 2007, and is an attending at Wilford Hall Medical Center in San Antonio, Texas. Shown here, in Iraq, he was scheduled to be deployed to Air Force Theater Hospital in Balad, Iraq, in January.





Rima Nasrallah Rusnak, M.D., MD'02, and her husband, Kevin, welcomed a son, Joey, on Aug. 31, 2006. She has completed her pediatric residency and chief residency at Cincinnati Children's Hospital Medical Center, and is now in her second year as a staff physician in the emergency department at Cincinnati Children's.



Attending a Young Alumni event in Chicago, are (left to right): Airron Richardson, M.D., MD'05, Rami Lutfi, M.D., Lisa Jackson, M.D., MD'03, and Chloe Rowe, M.D., MD'03.

Center. Busam is well known in Elder – he was the 1993 Elder High School valedictorian and member of the state champion basketball team. He and his wife, Mollie, have two children.

Coley Bryant Duncan, M.D., FE'03-'07, has completed a fellowship at Vanderbilt and is now an assistant professor of Medicine in the Division of Infectious Diseases/Department of Medicine at the University of Rochester in Rochester, N.Y.

Kristin Ehst, M.D., MD'03, HS'03, has completed her internal medicine and pediatrics residency at Vanderbilt is now pediatric chief resident.

Darcie Gorman, M.D., MD'04, and Troy Gorman, M.D., MD'04, are both at the University of Utah in Salt Lake City. Darcie is currently chief medical resident and has matched at Utah for a gastroenterology fellowship; and Troy is in his fourth year of an orthopaedic surgery fellowship, and is applying for a fellowship in foot and ankle surgery.

Meri Todd Harper, M.D., MD'01, and her husband, Seth, welcomed a daughter, Grace Elizabeth, on Aug. 4. They are living in Salt Lake City where she is practicing pediatrics and her husband, family medicine.

Matthew Harris, M.D., MD'02, and his wife, Amber, married on May 19, 2007, in New Smyrna Beach, Fla.

Allan Moore, M.D., MD'03, has completed a fellowship in endocrinology at Massachusetts General Hospital, and is enrolled in the Masters in Medical Science Program at Harvard Medical School. He has also joined the Vanderbilt Medical Alumni Association board of directors, and married Rebekah Gee in 2006. She is completing a Robert Wood Johnson Fellowship.

Frank Mullens, M.D., MD'00, is working as a staff radiologist at Yokosuka Naval Hospital, about 25 miles south of Tokyo.

Kelsey Hamilton O'Brien, M.D., HS'02-'05, married James O'Brien, a U.S. Air Force C-130 pilot on May 5, 2007. He is stationed at Little Rock Air Force Base. She has joined the nine-physician Arkansas Pediatric Clinic.

Boris Pavlin, M.D., MD'03, has accepted a position as a medical epidemiologist for the World Health Organization, based in Pohnpei, Micronesia. He will be in charge of helping national governments in the region develop their capacity to detect and respond to emerging and epidemic-prone infectious diseases. On a personal note, he is engaged to Karien Stuetzle, his girlfriend of nearly three years.

Rima Nasrallah Rusnak, M.D., MD'02, has completed her residency and chief residency in pediatrics at Cincinnati Children's Hospital Medical Center, and is now a staff physician in the Emergency Department at Cincinnati Children's. She and her husband, Kevin, married in 2004 and welcomed their first child, Joseph Michael on Aug. 31, 2006.

Beth Atkinson Zow, M.D., MD'02, and her husband, Mark, welcomed their first child, Adam Christopher, on Jan. 4, 2007.

Carlos Arteaga, M.D., director of the Vanderbilt-Ingram Cancer Center Breast Cancer Program, has been named an American Cancer Society Clinical Research Professor. The honor includes a five-year, renewable grant and membership in the elite group of American Cancer Society professors. There are 20 Research Professors and 11 Clinical Research Professors, including the three new Clinical Research Professors selected this year.

Shari Barkin, M.D., chief of the Division of General Pediatrics at the Monroe Carell Jr. Children's Hospital at Vanderbilt, has been selected for an exclusive training program to groom women in medicine for high-ranking roles in academic leadership. Barkin is one of 47 physicians and only one of 10 pediatricians nationwide selected for this year's class of Executive Leadership in Academic Medicine (ELAM) Program for Women. ELAM fellows spend a year learning elements of leadership that are traditionally part of an MBA program with an orientation toward the health care business environment. They also develop and implement an institutional program tailored to enhance the mission of their institutions.

Rebecca Bauer, M.D., a resident in the Department of Orthopaedic Surgery, was recently chosen by Vanderbilt University School of Medicine students to receive the CANDLE (Caring, Advocating, Nurturing, Determination, Leadership and Empathy) Award. The honor is given to individuals who have devoted themselves to teaching and mentoring.

William Bernet, M.D., professor of Psychiatry and director of the Division of Forensic Psychiatry, has co-authored a book, "Children of Divorce: A Practical Guide for Parents, Therapists, Attorneys and Judges." It's unique among books for divorced parents because it blends the expertise of psychiatric and legal professionals.

***Andre Churchwell, M.D.**, assistant professor of Medicine and a cardiologist with the Vanderbilt Heart and Vascular Institute, has been named associate dean for Diversity in Graduate Medical Education and Faculty Affairs.

***Kevin B. Churchwell, M.D.**, a Nashville native, Vanderbilt-educated physician and nationally recognized pediatrician, has been named chief executive officer and executive director of the Monroe Carell Jr. Children's Hospital at Vanderbilt. He held the interim position since January, when he replaced the

hospital's first CEO, **Jim Shmerling**, who left to become president and CEO of The Children's Hospital of Denver.

James Crowe Jr., M.D., professor of Pediatrics, won a Chancellor's Research Award for two publications on human metapneumovirus infections in children. He received the award at the University Fall Faculty Assembly.

Utpal Davé, M.D., assistant professor of Medicine and Cancer Biology, has been chosen to receive a Doris Duke Clinical Scientist Development Award to study the role of the HTLV-1 retrovirus in Adult T-cell leukemia, one of the few malignancies caused by a retrovirus. The Doris Duke Clinical Scientist Development Awards are designed to prepare and support new investigators as they begin their careers as independent clinical researchers. Recipients receive \$135,000 per year for three years.

Sean Davies, Ph.D., research assistant professor of Pharmacology, is among the first group of scientists to receive the NIH Director's New Innovator Award. He has a novel idea that could eliminate the daily drug intake required to treat chronic diseases. And now he has five years of funding from the National Institutes of Health to develop and test that idea. The program was launched to support new investigators with bold research proposals that could have great impact on biomedical or behavioral science. Davies is one of 29 awardees who will receive \$1.5 million in direct costs over five years. More than 2,100 investigators applied for the awards.

Terence Dermody, M.D., has been named a Fellow of the American Association for the Advancement of Science (AAAS), an honor bestowed upon AAAS members by their peers. Dermody, a professor of Pediatrics, professor of Microbiology and Immunology, director of the Elizabeth B. Lamb Center for Pediatric Research, and director of the Vanderbilt Medical Scientist Training Program, was honored for his "distinguished contributions to the field of virology and viral pathogenesis, particularly for studies of reovirus attachment, cell entry and innate immune response signaling."

Nick Desai, M.D., has received one of eight educational seed grants in support of innovative ideas in teaching and learning. Desai's proposal was: "An Online Curriculum for Adolescent Medicine Vanderbilt University School of Medicine."

***Ronald Emeson, Ph.D.**, Joel G. Hardman Professor of Pharmacology. Blakely is the Allan D. Bass Professor of Pharmacology, has been named deputy director of the Center for Molecular Neuroscience (CMN). In the newly created position, he will assume responsibility for maintaining and expanding the center's research resources, and will launch a new Program in Nervous System Engineering.

Richard Fremont, M.D., and ***Lorraine Ware, M.D.**, have received one of eight educational seed grants in support of innovative ideas in teaching and learning. Their proposal was: "A Case-Based Online Curriculum for More Uniform Education in the Medical Intensive Care Unit."

Joseph Gigante, M.D., and ***Rebecca Swan, M.D.**, have received one of eight educational seed grants in support of innovative ideas in teaching and learning. Their proposal was: "A Simplified Observation Tool for Pediatric Residents in Continuity Clinic."

Nunzia Giuse, M.D., M.L.S., professor of Biomedical Informatics and director of Eskind Biomedical Library, received the President's Meritorious Service Award from Meharry Medical College. The award comes at the midpoint of a five-year Meharry-Vanderbilt Alliance initiative to assist modernization of the Meharry Library.

Luke Gregory recently joined Vanderbilt University Medical Center as assistant vice chancellor for Health Affairs, senior vice president, and chief business development officer. Gregory's position combines components of those formerly held by ***Norman Urmey** and ***Jeff Kaplan**. A longtime Nashvillian, Gregory was formerly CEO for Blakeford, Inc., a senior housing and health care company. His other jobs have included senior vice president at Baptist Hospital and Northeast Georgia Health System; vice president for business development at LifeTrust America, an assisted living company; and consultant with Clayton Associates, a health care venture capital company.

Dennis Hallahan, M.D., professor and chair of Radiation Oncology, has been named to the American Society for Therapeutic Radiology and Oncology's 2007 class of ASTRO Fellows. Hallahan and 39 other new fellows received their awards at a special ceremony during the 49th Annual Meeting in Los Angeles. Members of ASTRO are eligible to become a Fellow based on length of membership in the organization, leadership in the organization and contributions to the field of radiation oncology.

***Heidi Hamm, Ph.D.**, chair of the Department of Pharmacology, has been appointed to the Peer Review Advisory Committee of the National Institutes of Health (NIH). The committee advises the NIH director and other top NIH officials on the evaluation of NIH grant applications. Peer review, NIH officials said, "is the key method NIH uses to ensure that the \$20-plus billion it invests in biomedical research grants each year advances the most promising research."

Margaret Head, M.S.N., M.B.A., R.N., has been named chief operating officer of Vanderbilt Medical Group (VMG). Head succeeds David Posch, who in January became chief executive officer of The Vanderbilt Clinic and executive director of VMG. She comes to Vanderbilt from the Kelsey-Seybold Clinic — a private, 300-doctor multi-specialty group practice with 18 locations in Houston.

John Huff, M.D., has joined Vanderbilt University Medical Center as chief of the Section of Breast Imaging and imaging director for the Vanderbilt Breast Center. Huff, one of the region's most prominent clinicians, previously served nearly 15 years as director of Breast Imaging for Baptist Hospital, where he helped establish a medical advisory group, including several spe-

cialties involved in detecting and treating breast cancer and related diseases.

T. Alp Ikizler, M.D., associate professor of Medicine, has been named the Catherine McLaughlin Hakim Associate Professor of Medicine. The Catherine McLaughlin Hakim endowed chair honors the late Cathy Hakim, who died of metastatic breast cancer several years ago. She was married to Raymond Hakim, M.D., adjunct professor of Medicine, who was on the full-time faculty in the Division of Nephrology from 1987 to 1996.

***David Johnson, M.D.**, director of the Division of Hematology/Oncology and deputy director of the Vanderbilt-Ingram Cancer Center, has received the Clinical Researcher Award from the Association of Community Cancer Centers (ACCC). The annual research award is given to an individual whose research has significantly and positively impacted the oncology patient, family and community. Johnson was honored during the national ACCC Oncology Economics Conference in Dallas.

Jim Lawson, deputy director of the Meharry-Vanderbilt Alliance, has been recognized for his 15 years of service on the Metropolitan Nashville Planning Commission. A certificate was presented to Lawson at the Metro Council meeting in July. The Planning Commission is responsible for determining the design standards and development plans — both commercial and residential — for Nashville and Davidson County. Lawson was appointed to a four-year term on the Commission in 1992 by Mayor Phil Bredesen.

Amy Major, Ph.D., assistant professor of Medicine and Pathology, recently received the Irvine H. Page Young Investigator Research Award in recognition for her leadership in cardiology research. Major was one of 50 applicants who submitted manuscripts. Her work was highlighted during the 7th Annual Council on Arteriosclerosis Thrombosis and Vascular Biology Conference.

Ingrid Mayer, M.D., assistant professor of Hematology/Oncology, is one of the inaugural recipients of the 2007 Grants in Translational Breast Cancer Research from the Breast Cancer Research Foundation (BCRF) and the American Association for Cancer Research (AACR). The two-year, \$233,333 grants provide direct support for innovative breast cancer research projects designed to accelerate the discovery, development and application of new ways to treat breast cancer, or for preclinical research with direct therapeutic implications.

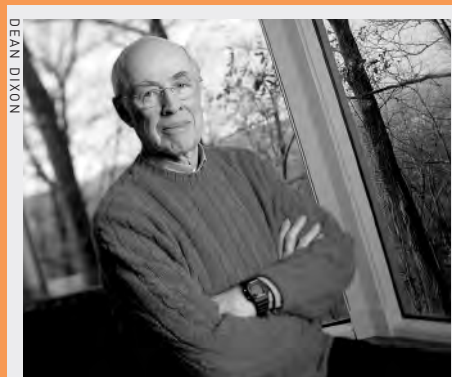
***Steven Meranze, M.D.**, and ***Marta Hernanz-Schulman, M.D.**, have been named vice chairs of the Department of Radiology and Radiological Sciences. The position was formerly held by Jeremy Kaye, M.D., who was named chair of the department in March. A specialist in vascular and interventional radiology, Meranze will serve as vice chair of Radiology for the adult hospital and clinics. Hernanz-Schulman, a pediatric radiologist, will serve as vice chair of Radiology at the Monroe Carell Jr. Children's Hospital at Vanderbilt.

Sumi Misra, M.D., **Mohana Karlekar, M.D.**, **James Bridges, M.D.**, **Ralf Habermann, M.D.**, **Melinda Henderson, Barbara Murphy, M.D.**, and ***James Powers, M.D.**, have received one of eight educational seed grants in support of innovative ideas in teaching and learning. Their proposal was: "An Innovative, Holistic, Interdisciplinary, Multi-Site, Palliative Care-Based Approach to Train Medical Students to Care for Patients Facing Advanced Illness and Death Across the Continuum of Care."

***James A. O'Neill Jr., M.D.**, J.C. Foshee Distinguished Professor of Surgery, Emeritus, at the Monroe Carell Jr. Children's Hospital at Vanderbilt, received the William E. Ladd Medal at the 2007 National Conference of the American Academy of Pediatrics in San Francisco. The award, established in 1954, recognizes an individual who has significantly advanced the surgical care of children. The Ladd Medal was named in honor of William E. Ladd, M.D., considered the father of pediatric surgery in the United States. Only 32 Ladd Medals have been given since the award's inception.

Melinda New, M.D., has received one of eight educational seed grants in support of innovative ideas in teaching and learning. Her proposal was: "An Online Ob/Gyn Curriculum in Ambulatory Care."

***Robert Ossoff, M.D.**, the Guy M. Maness Professor of Otolaryngology and chair of the Department of Otolaryngology, is transitioning from his role as director of the Vanderbilt Bill Wilkerson Center for Otolaryngology and Communication Sciences, effective next June, after a storied career spanning 22 years of assisting patients with speaking and singing problems. Ossoff will become assistant vice chancellor for Compliance and Corporate Integrity after ***James Snell, M.D.**, retires in December 2008. During his tenure Ossoff brought Music City and its A-list of singers and entertainers a Voice Center that ranks among the finest in the nation.



***John Oates, M.D.**, the Thomas F. Frist Professor of Medicine and professor of Pharmacology at Vanderbilt University Medical Center, has received the Lifetime Achievement Award from the Eicosanoid Research Foundation for his groundbreaking contributions to understanding the role of these potent molecules in health and disease. Oates received the award in September at the 10th International Conference on Bioactive Lipids in Cancer, Inflammation, and Related Diseases in Montreal. He also was a plenary speaker at the three-day conference, which was sponsored by the Detroit-based foundation.

Gregory Plemmons, M.D., has received one of eight educational seed grants in support of innovative ideas in teaching and learning. Plemmons' proposal was: "Telling Patient Stories: Narrative Medicine/Medical Writing."

***David Robertson, M.D.**, the Elton Yates Professor of Medicine, Pharmacology and Neurology, and director of the Elliott V. Newman Clinical Research Center, received one of Vanderbilt University's highest honors, the Earl Sutherland Prize for Achievement in Research, for "groundbreaking contributions" to understanding heart and blood pressure regulation. Robertson was honored during the University Fall Faculty Assembly.

Michael Rosen, M.D., a clinical fellow in Pediatric Gastroenterology at the Monroe Carell Jr. Children's Hospital at Vanderbilt, has been named the first recipient of the ***Thomas A. Hazinski, M.D.**, Scholarship by the Master of Science in Clinical Investigation (MSCI) Program. Hazinski, who died in January 2006, co-founded the MSCI program in 2000 and was actively involved in the curriculum. The Hazinski Scholarship was developed with the goal of providing tuition support to promising individuals who have dedicated themselves to patient-oriented research and applied to the MSCI Program. Award criteria include a dedication to patient-oriented research, excellence in research and outstanding mentorship and environment.

***Meg Rush, M.D.**, has been named chief of staff and ***Paul Hain, M.D.**, has been named associate chief of staff for the Monroe Carell Jr. Children's Hospital at Vanderbilt. Rush and Hain succeed ***Kevin Churchwell, M.D.**, who was named chief executive officer for Children's Hospital in August after serving as chief of staff for two years. Previously, Rush and Hain served as interim chiefs of staff.

Jeffrey Samz has been appointed the newly created position of chief executive officer of the Vanderbilt Heart and Vascular Institute (VHVI). Samz comes to Vanderbilt from Duke University Hospital, where he is the associate operating officer for Heart Services, a position he has held since 2005.

Harriette Scarpero, M.D., **Derenda Gold, M.D.**, and ***Joseph Smith, M.D.**, have received one of eight educational seed grants in support of innovative ideas in teaching and learning. Their proposal was: "The Effect of Formal Mentoring Program on Competency Teaching and Assessment in Urology Training."

Beth Ann Sastre, M.D., ***Anderson Spickard III, M.D.**, and **Josh Denny, M.D.**, have received one of eight educational seed grants in support of innovative ideas in teaching and learning. Their proposal was: "Teaching Evidence-Based Medicine: Searching Skills."

***William Schaffner, M.D.**, chair of the Department of Preventive Medicine, was recently elected to serve on the executive committee of the Board of Directors of the Infectious Diseases Society of America (IDSA) as the organization's secretary. He will serve a term of three years. As secretary, Schaffner will have oversight to the National and Global Public Health Committee, as well as to the Immunization Work Group — a body working with Congress to improve access to vaccines for children and adults. Schaffner was also one of two physicians honored by the VZV Research Foundation for their contributions to the fight against varicella zoster virus (VZV), which causes chicken pox and, later in life, the painful disease shingles.

Virginia Shepherd, Ph.D., professor of Pathology and director of the Vanderbilt Center for Science Outreach, shared the Thomas Jefferson Award for Distinguished Service with **Matthew Ramsey, Ph.D.**, associate professor of History, at the University Fall Faculty Assembly.

Josh Smith, M.D., a general surgery resident working to obtain his Ph.D. in Cell and Developmental Biology, has received the 2008-2009 Society of University Surgeons-Ethicon Scholarship Grant Award. He will appear before the Scientific Session of the 2011 Academic Surgical Congress Meeting to provide a final report on his research. Smith's research topic centers on the role of TGF-beta/Smad signaling in colorectal cancer, epithelial to mesenchymal transition (EMT) and the importance of the loss of Smad4 in relation to eventual clinical outcome. Smith also received an "Excellence in Research" designation for his presentation at the American College of Surgeons meeting in New Orleans in October.

C. Michael Stein, M.D., professor of Medicine and Pharmacology and associate director of Clinical Pharmacology at Vanderbilt University Medical Center, has been named the first holder of the newly endowed Dan May Chair in Medicine. Named for the prominent Nashville businessman, civic leader and lifetime member of the Vanderbilt Board of Trust who died in 1982, the Dan May chair is a gift from his late wife, Dorothy Fishel May, their son Joseph "Jack" May and his wife, Lynn Hewes May, of

Nashville, and their daughter, Elizabeth "Betsy" May Stern, and her husband, Walter Stern, of Scarsdale, N.Y. Stein, who joined the Vanderbilt faculty in 1993, is an expert on the genetic variability of drug responses, inflammation and atherosclerosis.

***Wendy Stone, Ph.D.**, professor of Pediatrics and a Vanderbilt Kennedy Center investigator, has been awarded the annual Outstanding Alumni Award from the Psychology Department at the University of Miami. Stone received her Ph.D. in Clinical Psychology from the University of Miami in 1981 and came to VUMC in 1988. She was instrumental in establishing the Vanderbilt Treatment and Research Institute for Autism Spectrum Disorders (TRIAD), which she also directs.

***Arnold Strauss, M.D.**, who served as chair of the Department of Pediatrics and medical director of the Monroe Carell Jr. Children's Hospital at Vanderbilt until March of this year, is one of 65 new members elected into the Institute of Medicine (IOM). Established in 1970 by the National Academy of Sciences, the Institute has become recognized as a national resource for independent, scientifically informed analysis and recommendations on human health issues. Members are elected by other members, and the IOM's total membership is now 1,692.

S. Bobo Tanner, M.D., assistant professor of Medicine in the Division of Rheumatology and the Division of Allergy and Immunology, has been named the Clinician of the Year by the International Society for Clinical Densitometry (ISCD) for his distinguished service to the study and practice of bone densitometry, a field that uses bone density measurement to predict, diagnose and treat osteoporosis. The Clinician of the Year Award plaque is given annually to one physician who is nominated and voted on by the ISCD nominating committee.

John Williams, M.D., assistant professor of Pediatric Infectious Diseases, received the 2007 Young Investigator Award from the Pediatric Infectious Diseases Society. The award honors and recognizes young physicians beginning a career in pediatric research for outstanding contributions in clinical or basic research in pediatric infectious diseases. Williams and his team have been investigating the epidemiology and immunology of human metapneumovirus and other respiratory viruses.

***F. Tremaine Billings, M.D.,** HS'39-'42, FA'60-07, professor of Medicine Emeritus at Vanderbilt University Medical Center and a member of the Vanderbilt faculty since 1941, died Sept. 16, 2007. He was 95. Dr. Billings, known to his friends as Josh, was a 1933 graduate of Princeton University, received his medical degree from Johns Hopkins University in 1938, and did his medical training at Johns Hopkins and Vanderbilt, where he was chief resident of Medicine. After World War II, he practiced internal medicine at Vanderbilt and served as the dean of Medical Students, associate dean for Medical Center Development Programs, and helped develop a health program for rural areas in Appalachia. He was instrumental in forming the partnership between VUMC and Meharry Medical College, and served as chair of Meharry's Department of Medicine from 1953-1961. His ties to Princeton remained strong all his life, where, as class secretary for the Class of 1933, he supplied Princeton Alumni Weekly with regular updates on his classmates.

Joseph M. Bistowish Jr., M.D., FA'65-'88, died Aug. 31, 2007, in Nashville. He was 87. He began his career in public health in 1947,

serving as assistant health officer at the State Board of Health Training Center in Gainesville, Fla. In 1964, he became director of health for the newly formed Metropolitan Government of Nashville and Davidson County, and retired from that position in 1987. He is survived by a daughter, Gwenn, and two grandchildren.

Walter Lee Bourland, M.D., HS'52-'56, died Nov. 8, 2007. He was 82. He practiced obstetrics/gynecology in Tupelo, Miss., from 1956 until 1989. Upon retirement he was a professor in the Department of Obstetrics and Gynecology at the University of Mississippi Medical Center. He was also instrumental in forming the Antoine Tannehill Good Samaritan Free Clinic, serving as its medical director from 1992-1997. He is survived by his wife, Martha; four children – Walter Lee Jr., M.D., John, Beth, and Katie; and 12 grandchildren.

Gregory Braden, M.D., FE'87-'89, died Aug. 13, 2007. He was 50. An interventional cardiologist in Winston-Salem, N.C., he served as director of Cardiovascular Research at Bowman Gray School of Medicine, Director of the Cardiac Cath Lab at Forsyth Memorial Hospital, and was head of Cardiology Specialists of North

Carolina. He is survived by his wife, Marion; four children – Jenny, Sarah, Amy and Drew; two stepchildren -- Travis and Heather; and three grandchildren.

C. Dale Brown, M.D., HS'66, CF'79-'84, died May 20, 2007. He was 67. For 30 years Dr. Brown was a radiologist at Western Baptist Hospital and Lourdes Hospital in Paducah, Ky., and also served as assistant professor of Radiology at the University of Kentucky and Vanderbilt for many years. He was the founder and medical director of the School of X-Ray Technology at Paducah Community College. He is survived by his wife, Cecilia; three sons – Michael, Scott and Stewart; and five grandchildren.

Robert Edward Burr, M.D., MD'61, HS'61-'63, FE'63-'64, HS'64-'66, died July 22, 2007. He practiced pediatrics in the Madison-Rivergate area of Nashville from 1968-1982, was chief of pediatrics at King Fahad Hospital, Riyadh, Saudi Arabia, from 1982-1984, and was a medical director for managed care at HCA and Equicor from 1984-1987. Until his retirement he was a private consultant for local, state and international managed care companies and a consultant for Social Security disability services. He is survived by his wife, Marie; daughters Lydia, Laurie; and two granddaughters.

G. Rodman Davenport, M.D., CF'63-'89, died June 3, 2007. He was 76. He is survived by his wife, Mary Jo; first wife, Eleanor; three daughters – Cathy, Jolene and Stephanie; and three grandchildren.

John Wolcott Garrett, M.D., MD'69, HS'69-'70, died May 13, 2007. He was 63. He became board certified in family practice in 1977 and practiced family medicine with privileges in obstetrics in Cowansville, Pa., until 1989. He completed training in obstetrics and gynecology in 1991, and opened his ob/gyn practice on the campus of the Armstrong County Medical Hospital. In 1994, he

became board certified in ob/gyn, continuing his solo practice until December 2005 when he retired. He is survived by his wife, Marian; his mother, Patty; a son, David; daughters, Heather and Christine; and six grandchildren.

***Richard Green, M.D.,** MD'49, died Sept. 28, 2007. He was 80. A former surgeon at Rutherford Hospital and Chief of Rehabilitative Medical Services at the Alvin York Veterans Administration Hospital in Murfreesboro, Dr. Green lived in Woodbury, Tenn. He is survived by his children, Libby, John and Sumner, and six grandchildren.

George A. Gross, M.D., MD'47, died Sept. 24, 2007. He was 84. He lived in Placida, Calif., and had a thriving psychiatric practice for 40 years in Sacramento, retiring when he was 80. He was a distinguished life fellow of the American Psychiatric Association, and is survived by his wife, Vivian, and children, John Wesley, Susan and Thomas.

Charles M. Hargadon, M.D., HS'65-'68, died April 15, 2007. He was 76. He worked as an orthopaedic surgeon from 1968-1994, and is survived by his wife of 53 years, Martha Ann; children, Brian and Diane; seven grandchildren and a great grandson.

***Milton Lanier Harris, M.D.,** MD'46, died July 18, 2007. He practiced internal medicine in Baton Rouge from 1952 to 1987, and was a diplomat of the American board of Internal Medicine and a fellow of the American College of Physicians. He is survived by his wife, Nita; sons, Shelby and Milton Jr., M.D.; and four grandchildren.

Helen Johnston, M.D., MD'35, HS'36-'37, died June 2, 2007. She was 95. According to her obituary, she was the first female to serve on the house staff at Vanderbilt, and spent most of her career in Jackson, Tenn., where she and her husband began a joint medical practice in 1942. She retired

***John Settle Johnson, M.D.,** MD'61, HS'61-'62, died Oct. 12, 2007, after battling ALS. A graduate of both Vanderbilt University and VUSM, he spent his early career at the National Institutes of Health, first as a clinical associate in the Arthritis and Rheumatology Branch of the NIH, and then as a senior investigator. He was an associate member and chief of Rheumatology at Scripps Clinic and Research Foundation in LaJolla, Calif., and returned to Nashville in 1974 to practice clinical medicine and rheumatology at Medical Specialists of Nashville. In 1995, he joined the full-time Vanderbilt Department of Medicine faculty, and served as Chief of Medicine at Saint Thomas Hospital for nine years. At Vanderbilt he was a recipient of the Hugh J. Morgan Teaching Award, the T. Leonard Tow Humanism Award "for the outstanding faculty role model of Vanderbilt University Medical School in recognition of exemplary compassion, competence and respect in the delivery of care," and the first John Settle Johnson Mentorship Award at VUSM, inaugurated by the VUSM Class of 2003. He was honored with the Masters award from the American College of Rheumatology in 2003. He is survived by his mother, Frances; his wife, Ellen; children, Margaret and Frances; and six grandchildren.

from her pediatric practice in 1954 to devote all of her time to her three children and her volunteer commitments. She is survived by children, Annie, Bill, M.D., and Lee, M.D.; eight grandchildren; and 10 great-grandchildren.

Greer Ricketson, M.D., CF'53-'07, died in August 2007, in Nashville. He was 90. Ricketson, a decorated World War II veteran, was a Nashville surgeon, but perhaps his most well-known role was as a Vanderbilt football player, when he carried the football to defeat previously undefeated Louisiana State University.

Robert Eugene Schell, M.D., MD'40, HS'40-'42, died April 2, 2007, in Asheville, N.C. He was 90. He served in the U.S. Army from 1941 to 1947, achieving the rank of major, and continued his career as head of Admissions and Outpatient Services at Morre General VA Hospital, and retired in 1980 from Oteen VA Hospital. He is survived by Mildred, his wife of 63 years; children, Pamela, Joan, Robert Jr. and Peggy; and six grandchildren.

Gisela K. Schuller, M.D., HS'64-'68, FA'70, died July 24, 2007. She was 85. She immigrated to the United States in 1950 and became an American citizen in 1956. In 1970, after serving on the Vanderbilt faculty, she moved to Tulsa, Okla., and practiced medicine there until she retired in 1995. She is survived by her sons, Stephen and Ralph, and five grandchildren.

Donald E. Schwarten, M.D., HS'67-'70, died Sept. 29, 2007, in Fishers, Ind. He was 66. He lived in the Indianapolis area for 26 years. He was a leader in developing interventional vascular and coronary techniques and performed the first coronary balloon angioplasty at St. Vincent Hospital, where he practiced vascular radiology. He was a leading investigator of many medical devices and in 1999, left private practice to join Guidant's Endovascular Business in California as Chief Medical

Officer. He returned to private practice in Indianapolis in 2006. He is survived by his wife, Betty; two children, John and Kathryn; and a grandson.

***John W. Simpson, M.D.**, MD'32, HS'33-'38, died April 25, 2007, in Kansas City, Mo. He was 100. Following his graduation from Vanderbilt, he had a long and distinguished career in both military and civilian medicine. He is survived by his daughters, Mary and Elizabeth; six grandchildren and five great grandchildren.

Walter M. Tasem, M.D., HS'44, died in May 2007. He began practicing pediatrics in 1947 and moved to Kaiser Permanente in 1967.

Dale L. Taylor, M.D., HS'62-'64, died Sept. 17, 2007, in Winter Haven, Fla. He was 70. He was a partner at the Watson Clinic in Lakeland, Fla., until his retirement in 1994, but continued to work there until 2003, assisting with quality and risk management initiatives. The first doctor in Polk County to perform laparoscopic surgery and to surgically reverse tubal ligations, he was a recipient of the American College of Obstetricians and Gynecologists' Outstanding District Service Award, and in 2007, received the first ACOG District IV Lifetime Achievement Award. He is survived by his wife, Lisa; children, Christopher, Andrew, Marybeth; stepchildren Thomas, Elizabeth and Shannon; and one grandchild.

Charles R. Thompson Jr., M.D., MD'56, died Aug. 25, 2007. He was 78. He was a surgeon in Seattle from 1961-1972, began private practice in Aberdeen in 1967, and retired in 1994. He is survived by his wife, Carol; children, Leslie, Lisa, Charles and Paige; and five grandchildren.

Benjamin James Wilson, Ph.D., FA'64-'88, died July 4, 2007. He was 84. While at Vanderbilt he participated in a five-week nutrition survey of the people of Nigeria, sponsored by the National Institutes of Health, and

was recognized as an authority on toxic substances occurring naturally in various foods consumed by humans, pets and farm animals. He is survived by his wife, Nancy; children, Suzanne, Barbara, Rebecca and James; and two grandchildren.

Sorrell L. Wolfson, M.D., MD'54, HS'54-'55, died Sept. 2, 2007. He was 80. A renowned pediatrician

ticed orthopaedic surgery in San Jose, Calif., for 20 years, and at Group Health of Puget Sound. He retired in 1989. He is survived by his wife, Virginia; children Robert III., M.D., John Thomas, and Virginia; and several grandchildren.

Herman Zaiman, M.D., MD'57, died Sept. 10, 2007, in Valley City, N.D. He was 89. An aviator with

Gail Addlestone, M.D., MD'97, may have been only 37 when she died on July 22, 2007 after an extended battle with cancer, but she made quite an impact during her too-short life.

Addlestone practiced pediatrics with Heritage Pediatrics, a group of Nashville pediatricians who are all Vanderbilt Medical School graduates. She was the "complete package," says her friend and colleague **Robert Mallard, M.D.**, MD'74, HS'75-'77. "She was the real deal. She wasn't just a friend or a physician or a community advocate. She was all of that in one person. She was so dedicated to her patients, and their families. She was a complete pediatrician, and dealt with much more than just the physical part of a child's problems. She had a real people gift, and knew how to comfort people. If a mom had a problem, she knew she had to help the mom if she wanted to help the child. If you interviewed 100 of her families, each would have different insights about Gail, but they would all say, 'wow, this is an exceptional person.'"

Mallard said despite her young age, physicians in the group sought her out for opinions and advice. "She could be dealing with 10 major problems, and if someone walked in the room with a problem of their own, she would help you. She was a huge, magnanimous kind of person."

She is survived by her husband, Jeffrey, and daughter, Eleanor.

and hematologist, he served as head of Pediatrics at Tampa General Hospital prior to the opening of the USF Medical School, and was devoted to studies in diagnostics and treatment of children's cancer as well as blood disorders including sickle cell anemia and hemophilia. He did extensive study in the area of children's poisoning and spearheaded the removal of products containing Parathion from homes. Survivors include children, Aaron, Mark, David, Sharon, and seven grandchildren.

Robert Walker Youngblood Jr., M.D., MD'47, HS'47-'49, died in May 2007, in Medford, Ore., He was 83. He served in U.S. Air Force, including several years in Wiesbaden, Germany, and prac-

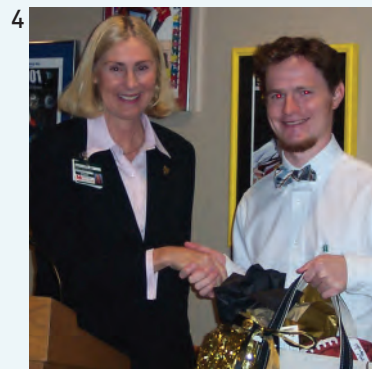
the U.S. Navy in World War II, he taught parasitology at Einstein College in New York City for many years, and was the author of medical textbooks on parasitology. He later went into private practice and moved to Minnesota and then to Valley City in 1984. He retired in 2000. He is survived by his children, Leslie, Kit, Karin, Richard, Stevan and Stuart; 13 grandchildren and three great-grandchildren.

Alumni Events

Pictured below:

1. The Vanderbilt Medical Alumni Association hosted a dinner at Brennan's Restaurant in New Orleans for members of the Scott Society in conjunction with the American College of Surgeons 93rd Annual Clinical Congress. Enjoying the dinner are: Leigh Phay, John Phay, M.D., FA '02-present, and Rachel Idowu, M.D., HS'04-'07.

2. William Lea, VUSM Class of 2008, attended the dinner at Brennan's with his father, John Lea IV, M.D., MD'77, HS'77-'84.



3. David Hout, Ph.D., Post Doctoral FE'07, and Anthony Baucum II, Ph.D., Post Doctoral FE'07, attended the Post Doc Picnic held in September near Vanderbilt.

4. Ann Price, M.D., executive director of the Vanderbilt Medical Alumni Association, gives Miles Foltermann, M.D., HS'07, the "Grand Prize Football Package" at October's VMAA Open House during Vanderbilt Reunion/Homecoming 2007.

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