

Unsurpassed Support for Pelvic Floor **Disorders FY11** Philanthropy Report

THE NEXT FRONTIER of Prenatal Genetics

Patient Turned Leader GIVING HAS REWARDS

Solving the Puzzle of PRETERM BIRTH



VOLUME 3 | WINTER 2011 | PHILANTHROPY REPORT

Magee is published three times a year for supporters of Magee-Womens Research Institute & Foundation (MWRIF).

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Please email info@mwrif.org if you no longer wish to receive fundraising materials designed to support MWRI and Magee-Womens Hospital of UPMC.

Thank you for your continued support of Magee-Womens Research Institute & Foundation.





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Women suffering from pelvic floor disorders count on Magee for first-rate care. The urogynecologic community counts on it for first-rate research.

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MWRI is on a mission to improve prenatal genetic testing — and the peace of mind of parents-to-be.

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Magee Newsmakers

Recent Publications and Abstracts

[OCTOBER 2011]

Vaginal cuff dehiscence after different modes of hysterectomy

Hur HC, Donnellan N, Mansuria S, Barber RE, Guido R, & Lee T

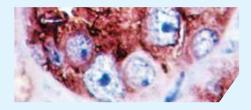
Obstet Gynecol, 118:794-801 PMID: 21934442

[SEPTEMBER 2011]

Periconceptional multivitamin use and risk of preterm or small-forgestational-age births in the Danish National Birth Cohort

Catov JM, Bodnar LM, Olsen J, Olsen S, & Nohr FA

Am J Clin Nutr, 94(3):906-12 PMID: 21795441



[AUGUST 31, 2011]

Forkhead box A1 (FOXA1) is a key mediator of insulin-like growth factor I (IGF-I) activity

Potter AS, Casa AJ, & Lee AV J Cell Biochem, doi: 10.1002/jcb.23333 [Epub ahead of print] PMID: 21882221

[AUGUST 10, 2011]

Evidence from the agonadal juvenile male rhesus monkey (Macaca mulatta) for the view that the action of neurokinin B to trigger gonadotropin-releasing hormone release is upstream from the Kisspeptin receptor

Ramaswamy S, Seminara SB, & Plant TM

Neuroendocrinology [Epub ahead of print]

PMID: 21832818

[JUNE 2011]

Pharmacokinetics of oseltamivir among pregnant and nonpregnant women

Beigi RH, Han K, Venkataramanan R, Hankins GD, Clark S, Hebert MF, Easterling T, Zajicek A, Ren Z, Mattison DR, Caritis SN, & Obstetric-Fetal Pharmacology Research Units Network

Am J Obstet Gynecol, 204(S1):S84-8 PMID: 21492826

[MAY 15, 2011]

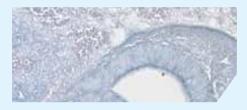
Phase 1 randomized trial of the vaginal safety and acceptability of SPL7013 gel (VivaGel) in sexually active young women (MTN-004)

McGowan I, Gomez K, Bruder K, Febo I, Chen BA, Richardson BA, Husnik M, Livant E, Price C, Jacobson C, & MTN-004 Protocol Team AIDS, 25(8):1057-64 PMID: 21505316

[MAY 2011]

Neuronal suppressor of cytokine signaling-3 deficiency enhances hypothalamic leptin-dependent phosphatidylinositol 3-kinase signaling

Metlakunta AS, Sahu M, Yasukawa H, Dhillon SS, Belsham DD, Yoshimura A, & Sahu A Am J Physiol Regul Integr Comp Physiol, 300(5):R1185-93
PMID: 2135649



[APRIL 2011]

First trimester uric acid and adverse pregnancy outcomes

Laughon SK, Catov J, Powers RW, Roberts JM, & Gandley RE

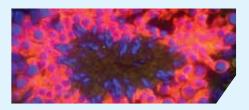
Am J Hypertens, 24(4):489-95 PMID: 21252861

[2011]

Energy metabolism in human pluripotent stem cells and their differentiated counterparts

Varum S, Rodrigues AS, Moura MB, Momcilovic O, Easley CA 4th, Ramalho-Santos J, Van Houten B, & Schatten G PLoS One, 6(6):e20914

PMID: 21698063



[2011]

Performance of swabs, lavage, and diluents to quantify biomarkers of female genital tract soluble mucosal mediators

Dezzutti CS, Hendrix CW, Marrazzo JM, Pan Z, Wang L, Louissaint N, Kalyoussef S, Torres NM, Hladik F, Parikh U, Mellors J, Hillier SL, & Herold BC

PLoS One, 6(8):e23136 PMID: 21858008

For a complete list of recent publications, please visit www.mwrif.org/416.

Clinical Trial News

Preserving Fertility after Cancer

Principal Investigator: Kyle Orwig, PhD

PARTICIPATION: (Limited to)

- · Females age 1 to 40 with two ovaries
- Males older than 1 year old with two testes
- Patients with a newly diagnosed or recurrent disease that requires chemotherapy or radiation treatment and puts them at high risk for infertility



DESCRIPTION:

Magee-Womens Research Institute's Fertility Preservation Program (FPP) is conducting an experimental research study for patients facing chemotherapy or radiation therapies that can threaten fertility. For young patients who are not yet producing mature eggs or sperm, the FPP is approved to freeze testicular or ovarian tissue that might later be used to restore fertility.

COMPENSATION:

The FPP will cover the costs of surgery, tissue processing, tissue freezing, and the first year of frozen storage.

For more information, please call the FPP's dedicated phone line at 412.641.7475.

Biological Analysis of Fetal Nucleic Acids in Maternal Plasma

Principal Investigator: David Peters, PhD

PARTICIPATION: (Limited to)

Pregnant women and their partners (>18 years) who are undergoing chorionic villus sampling (CVS), amniocentesis, or a first trimester screen







DESCRIPTION:

The study is based on the finding that when a woman is pregnant, some of the baby's DNA travels into the mother's blood stream. The study will investigate whether blood samples obtained from pregnant women can be used to diagnose unborn babies with genetic disorders. A test of this nature could provide a new, noninvasive option for prenatal diagnosis.

Participation in this study requires a one-time blood donation (about 8 teaspoons).

If you are undergoing CVS or amniocentesis, we will obtain some of the extra cells that would normally be discarded afterwards. If you do not undergo CVS or amniocentesis, a small sample of the placenta or umbilical cord blood may be obtained after delivery of your baby. We may also review your medical records to obtain general information about the pregnancy outcome.

For more information, please call the Center for Medical Genetics at Magee-Womens Hospital of UPMC at 412.641.4168.

In the News

Stephen Emery, MD



Stephen Emery, MD, a maternal-fetal medicine specialist, was the subject of a September 15 KDKA TV story. The segment focused on his cutting-edge laser surgery for twin-to-twin transfusion syndrome, a rare and potentially deadly pregnancy complications.

Dr. Emery's twin-to-twin transfusion surgery was also featured on Discovery Channel's "Life Changing Medicine," an hour-long program about UPMC's medical innovations.



On the Honor Roll

UPMC was named to the *U.S. News & World Report* Honor Roll of America's Best Hospitals, ranking 12th among thousands of eligible hospitals. Magee-Womens Hospital of UPMC ranked 7th in gynecology, 42nd in orthopaedics, and 45th in cancer.

For the most up-to-date news and happenings, visit www.mwrif.org.

Rising Stars



Caroline Rieser, a second-year medical student at the University of Pittsburgh, received a merit award during the Dean's Summer Research Program symposium in October. She also presented a poster at the University of Pittsburgh's Science 2011 — Next Gen conference in October.

Expanding Upward: Magee-Womens Hospital Construction Update

The pouring of concrete roof and floor slabs for the Magee-Womens Hospital of UPMC expansion was completed in July. Since then, contractors have focused on installing the exterior of the addition and getting rooftop mechanical equipment into place. Mechanical, electrical, and plumbing work will continue through February.

"Our contractors have noted that everyone has been very understanding and shown patience," says Greg Gibala, senior project manager, Construction Management. "The physicians and staff deserve a much appreciated thank you."

The project will add two floors to the 800 Blue Zone area, increasing the number of beds by 42. One of the floors will hold a 14-bed intensive care unit (ICU). The expansion will help Magee meet increased demand for obstetrical and medical-surgical services.

The project is on target for substantial completion by May 2012.

MAGEE Magazine Around the World



Courtney Wickline, niece of Denise Wickline of Magee-Womens Foundation, poses with the inaugural issue of *MAGEE* magazine in front of the Coliseum in Rome, Italy.

We will be accepting photos like this for future magazine issues. Submit photos with captions to info@mwrif.org.

Recognizing Excellence



Aletha Akers, MD, MPH received a two-year \$207,055 R21 grant from the National Institutes of Health for her study "Relationship between adolescent weight, sexual behavior, and reproductive outcomes." The aim of the study is to identify the mechanisms underlying the observed associations between weight, sexual behavior, and reproductive outcomes among adolescents and identify subgroups of youth for whom these associations are strongest. The findings will facilitate tailoring of sex education, sexual risk reduction, and weight management programs to provide targeted

messages to high-risk youth.



Miriam Cremer, MD, MPH

received the second annual Contraception Associate Editors Outstanding Article Award for her article "Immediate vs. delayed post-abortal copper T 380A IUD insertion in cases over 12 weeks of gestation." The award recognizes the principal investigators who published the most outstanding articles in Contraception over the preceding academic year.



Sandra Founds, CNM, FNP, PhD

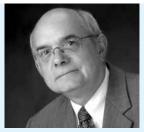
was one of two recipients of the Preeclampsia Foundation's 2011 Vision Grant. The prestigious award will fund her research to develop an early clinical screening test to help prevent preeclampsia.







Aleksandar Rajkovic, MD, PhD



W. Allen Hogge, MD

received a five-year \$2.8 million R01 grant from the National Institutes of Health for their study of non-invasive prenatal genetic testing. Their goal is to reduce miscarriages and other risks associated with amniocentesis and chorionic villus sampling, which are used to detect genetic abnormalities during pregnancy.



Jennifer Condon-Jeyasuria, PhD



Judith Yanowitz, PhD

have created a graduate-level lecture series called "Reproductive development from model organisms to humans" for the University of Pittsburgh. It includes 12 lectures by Magee-Womens Research Institute (MWRI) investigators. In September students were treated to a guest lecture by Stephen C. Stearns, PhD, of Yale University, who spoke on "The evolution of sex, sexual selection, and sexual conflict." The course, which runs through December 12, raises MWRI's visibility within the university community and will hopefully spark more collaborations.



- Rogier Donker, PhD, postdoctoral fellow, presented the poster "The C19MC microRNA profile in primary human trophoblast cells and exosomes."
- Yoel Sadovsky, MD, chaired the spotlight session "Embryonic development in animals and in humans."
- Yaacov Barak, PhD, and Judith Yanowitz, PhD, gave lectures during the session.
- · Adrian Lee, PhD, presented "Fingerprinting cancer genomes."



Gerald Schatten, PhD

and colleagues received a five-year \$1.6 million grant from the National Cancer Institute's Education Grant Program. The funding will be used to offer an annual advanced training course, "Frontiers in stem cells in cancer," for promising physician-scientists. It will also support pilot research projects and mentoring programs. The courses will be offered at Howard University in Washington, D.C., and at the Ponce School of Medicine and Health Sciences in Puerto Rico.



Pamela A. Moalli, MD, PhD



Hyagriv Simhan, MD, MS

are principal investigator and co-principal investigator, respectively, of the Impact of Pregnancy and Parturition on Pelvic Organ Support (I3POS) study, funded by a \$140,000 grant from the Jewish Healthcare Foundation. The study's overall goal is to understand the relative roles of first-time pregnancy and delivery in the mechanism by which pelvic organ prolapse occurs after delivery. The authors will also be able to determine for the first time whether Caesarean section prior to the onset of labor is protective against the development of pelvic organ prolapse or whether pregnancy itself confers an independent risk.

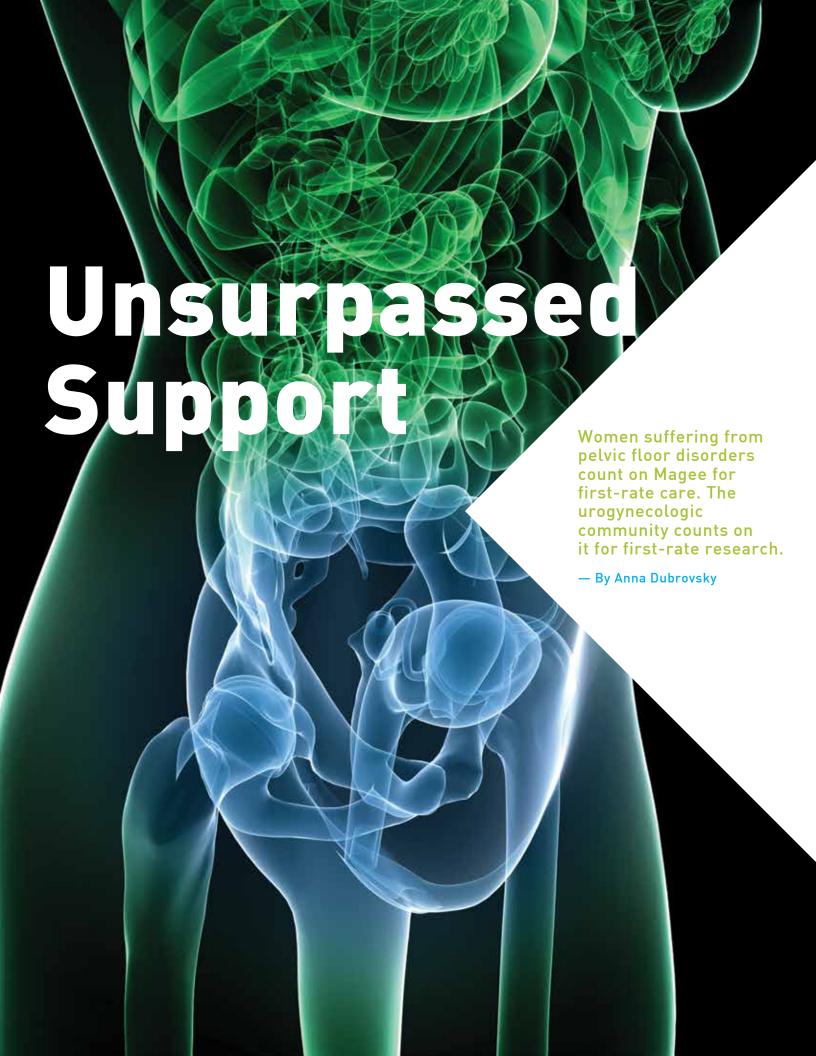
Highlights from the International Federation of Placenta Associations conference in Geilo, Norway, September 14 to 17:

Yoel Sadovsky, MD

- Chaired a mini symposium titled "Epigenetic and micro RNA-dependent gene regulation," during which he presented "The search for function of placental microRNAs."
- Presented "Trophoblastic lipid trafficking and accumulation" during a workshop titled "Roles of lipids in the growth and development of the feto-placental unit."
- Was named editor of the journal *Placenta*, effective January 1, 2012.

J. Richard Chaillet, MD, PhD

- Presented "DNMT1 enzymes and imprinting mechanisms."
- Gave a plenary session presentation titled "Imprinting and early placental development."



As medical director of the Women's Center for Bladder and Pelvic Health at Magee-Womens Hospital of UPMC, Halina Zyczynski, MD, sees something most doctors don't: a downside to exercise.

"The more physically active you are, the more symptomatic your urinary incontinence is going to be," she says. "Playing bridge rarely invokes incontinence. But going out there and power walking or doing Silver Sneakers or Jazzercise does." It's not unusual for women suffering from incontinence or other pelvic floor disorders to sacrifice their favorite pastimes — and the social interaction that comes with them.

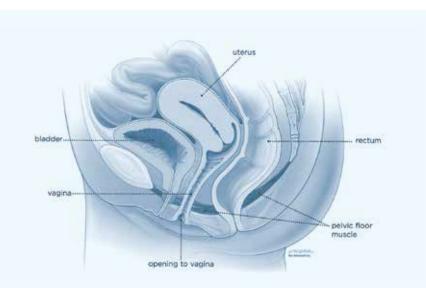
Dr. Zyczynski has devoted a quarter of a century to getting them back in the game. Thanks in part to her research and clinical work, Magee is recognized internationally as a leader in the field of female pelvic medicine and reconstructive surgery, a subspecialty of obstetrics and gynecology that's better known as urogynecology. Urogynecologists focus on the treatment of bladder and bowel control problems, pelvic organ prolapse, pelvic pain, and other pelvic floor disorders, which are exceedingly common. It's estimated that nearly half of all women between the ages of 50 and 79 have some form of prolapse, though far fewer experience bothersome symptoms. Urinary incontinence affects 30 to 50 percent of women.

In addition to causing physical pain or discomfort, pelvic floor disorders can exact a psychological toll ranging from embarrassment to depression. While breast cancer patients wear pink and walk en masse to raise awareness and money, women with pelvic floor disorders keep their problems mostly to themselves. "It's not exactly cocktail party conversation," Dr. Zyczynski says.

Fortunately, as Magee's reputation for successfully treating pelvic floor disorders has spread, more and more area women are seeking care. To meet demand, Magee has expanded its physician roster to include six urogynecologists and four urogynecologic fellows — up from two urogynecologists a decade ago — and made them available well beyond the hospital on Halket Street. Women can access their expertise

in half a dozen far-flung communities, including the North Hills, the South Hills, Irwin, and Erie. "We are striving to provide every woman in the region accessible, comprehensive, individualized, state-of-the-art treatments for pelvic floor disorders," Dr. Zyczynski says.

But Magee's reputation in urogynecologic circles rests on more than patient success stories. The hospital and its across-the-street neighbor, Magee-Womens Research Institute (MWRI), have produced some of the most valuable research in the field. "More than half of the women who have sought care through our center in the last decade have graciously participated in clinical trials," Dr. Zyczynski notes. MWRI is home to one of only three basic science laboratories dedicated to urogynecology in the country. At this year's scientific meeting of the American Urogynecologic Society, the lab's principal investigator, Pamela Moalli, MD, PhD, presented four papers to an audience of more than a thousand. Furthermore, Magee is one of eight clinical centers handpicked by the National Institutes of Health to participate in the Pelvic Floor Disorders Network, which conducts expansive studies. Drs. Zyczynski and Moalli serve as co-principal investigators in the network.



The Pelvic Floor

The pelvic floor is a set of muscles and connective tissues that support the pelvic organs, which in women include the bladder, rectum, vagina, and uterus. It's often described as a hammock.

Magee and MWRI are especially well known for their expertise in surgical mesh — a gauzy, porous material that can be used to reinforce the vaginal wall in cases of pelvic organ prolapse or to support the urethra to treat urinary incontinence. Magee clinicians use mesh in about one-third of procedures for pelvic organ prolapse and the vast majority of procedures for stress urinary incontinence, or leakage triggered by activities such as exercising, coughing, and laughing.

The Mesh Crisis

Mesh made headlines in July, when the U.S. Food and Drug Administration issued a warning about the surgical placement of mesh through the vagina to repair pelvic organ prolapse. The agency noted

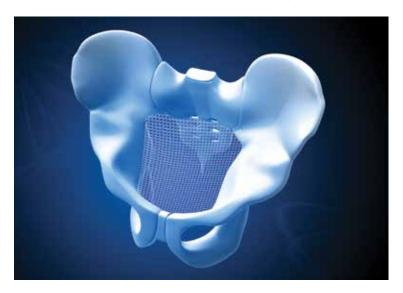
that serious complications are "not rare," adding that transvaginal repair with mesh may expose patients to greater risk than traditional non-mesh repair. It did not address use of mesh in prolapse surgeries performed through the abdomen, which are far more common at Magee, and reserved judgment on the use of mesh to repair stress urinary incontinence. But the warning turned mesh into a dirty word. "It has created anxiety among

women who have done well with mesh as recipients, who are now wondering: Was that a mistake? Will I have a problem in the future?" Dr. Zyczynski says. "It has created anxiety among those who are suffering with prolapse, have been counseled on their options, and may be best served by a mesh procedure." It has also created an atmosphere of litigation, prompting some doctors to avoid mesh altogether.

But women who do their homework will find that mesh-related complications are, in fact, well below published rates among Magee patients. That's because the hospital's urogynecologists are selective about which meshes they use and which patients they use them in. As sub-specialists, they also bring a great deal of training and experience to the table.

One of the reasons why complications are "not rare" in the general population is that many mesh procedures are performed by non-specialists, explains Dr. Moalli. "Fortunately, in the Pittsburgh area, most general ob-gyns refer their patients to the Women's Center for Bladder and Pelvic Health for these procedures. We spend all of our time doing urogynecology, and because of our narrow focus, we get highly skilled at what we do. In contrast, general ob-gyns spend a lot of time delivering babies, performing hysterectomies, and doing other gynecologic procedures, leaving limited time to invest in prolapse and incontinence surgeries." Research has shown that a doctor who performs a procedure several times a week will have better outcomes than one who performs it several times a year or even several times a month.

In addition, non-specialists don't necessarily understand what makes one mesh different from another and may be more susceptible to the sales pitches of mesh companies. "I can't tell you how hard vendors push you to use their product," Dr. Moalli says. "Not surprisingly, mesh information provided by a vendor is often riddled with bias, and the studies used to justify its use non-scientific."



Dr. Moalli has been sounding the not-all-meshes-are-equal alarm for years.

Thankfully, sales pitches are no match for Magee's research capabilities. Dr. Moalli's laboratory conducts extensive testing of currently marketed meshes. It is also developing a new mesh that is more compatible with the material properties of the vagina. "The ideal mesh has yet to be manufactured," says Dr. Moalli, who splits her time between patient care and lab work. "The major shortcoming is that current materials are inert and do nothing to improve the quality of the structurally compromised tissue in women with prolapse. What we are aiming to develop is a product that enhances the properties of the vagina so that it is restored to its uninjured, uncompromised condition."

Dr. Moalli has been sounding the not-all-meshes-are-equal alarm for years, and the surgical community is finally taking notice. Her presentation at the American Urogynecologic Society's scientific meeting in September "was really a 'wow' moment for much of the audience," says Dr. Zyczynski.

Among other things, Dr. Moalli showed the assembled crowd that stiffer meshes are more damaging to the vagina than lighter, more compliant ones. The stiffer the mesh, the more load it takes off the vagina. Without a load to bear, the vaginal tissue becomes lazy, to put it in laymen's terms. "This is counterintuitive to surgeons who were picking stiffer, stronger materials out of fear that their surgeries would fail. Unfortunately, stronger, stiffer meshes result in increased complications," Dr. Moalli says. Her research team observed decreases in smooth muscle, collagen, and other structural proteins following implantation with a stiffer mesh. Initially, she couldn't believe what they were seeing, having hypothesized that mesh implantation would stiffen vaginal tissue. "When they first showed me the results, I said, 'It has to be wrong. Do it again.' They repeated the experiments three times with the same results."

A Misquided Practice?

Dr. Moalli's other major research focus is on the causes of pelvic floor disorders. Giving birth vaginally is considered the leading risk factor for prolapse. That has given rise to the perception that Caesarean delivery will protect women against pelvic floor disorders later in life, which may be part of the reason why pre-labor Caesarean rates are climbing in the United States. But there's no scientific data to support that perception, and Dr. Moalli suspects that C-sections aren't truly protective. Because C-sections carry risks such as uterine rupture and abnormal attachment of the placenta to the uterine wall, she believes that offering Caesarean delivery as a means to prevent pelvic floor disorders is "an extreme and morbid" practice.

Thanks to funding from the Jewish Healthcare Foundation, she recently began a study to determine once and for all whether C-section prior to the onset of labor plays a protective role. She plans to follow 1,500 women during and after their first pregnancy, comparing the prevalence of prolapse in those who delivery vaginally, those who deliver by C-section after the onset of labor, and those who deliver by C-section before the onset of labor.

The study is also expected to shed light on the impact of age, race, body mass index, smoking, constipation, exercise level, and other factors on pelvic floor health.

Dr. Moalli will need further funding to complete the study, and she's crossing her fingers that the National



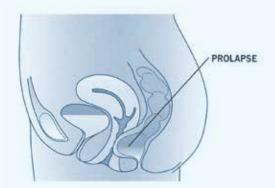
"Whether we're seeing patients or working in the laboratory, we're constantly striving to improve the quality of women's lives, and particularly the latter half."

Dr. Zyczynski

Institutes of Health (NIH) provides it. But pelvic floor disorders, common as they are, don't garner as much public attention or funding as, say, cancer or cardiovascular disease. "We're in a tough time for research," she says. "If you're in the NIH and you have to decide between funding a study on pelvic floor disorders or funding cancer research, cancer is going to win every time."

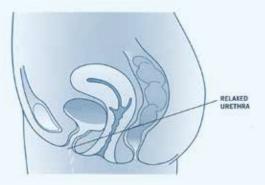
After all, cancer is a top killer. While oncologists focus on saving lives or at least prolonging them, urogynecologists focus on quality of life. "Whether we're seeing patients or working in the laboratory, we're constantly striving to improve the quality of women's lives, and particularly the latter half," Dr. Zyczynski says.

"My grandmother lived to be 101, and when a patient walks through the door, I always think of my grandmother," she adds. "They can be 55 years old, but I remember that they have the potential to live to be 101. So whatever intervention we recommend and ultimately perform should be durable and safe for when they're 101."



Pelvic Organ Prolapse

When the pelvic floor is weakened or damaged, one or more pelvic organs may prolapse (bulge) into the vagina. It's estimated that nearly half of all women between the ages of 50 and 79 have some form of prolapse, though far fewer experience bothersome symptoms.



Stress Urinary Incontinence

There are several types of urinary incontinence. Stress incontinence refers to urine leakage that occurs in the course of physical activities that increase abdominal pressure, e.g., exercising, sneezing, or laughing. It is thought to be caused by damage to the muscles and other tissues that close or provide support to the urethra.

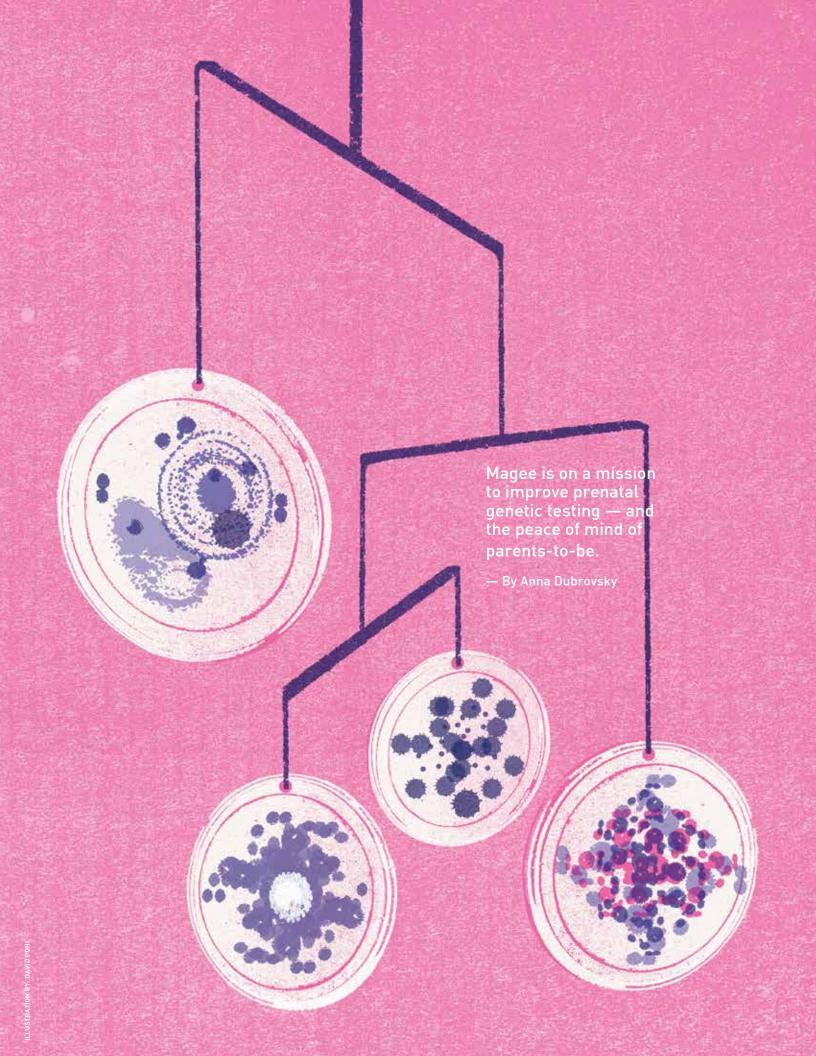
FLEX 'EM, LADIES!

If you've ever hit the gym, you know the benefits of exercise. But did you know it's possible to exercise the pelvic floor muscles, which support the bladder, bowel, and other pelvic organs? Strengthening these muscles through Kegel exercises can help you prevent or improve urinary incontinence and other pelvic floor disorders. It's important to identify the right muscles. Here are some tips from the American Urogynecologic Society:

- When urinating, try stopping midstream. If you succeed, you're working the right muscles. (Don't make a habit of stopping your urinary stream because it can lead to incomplete emptying of the bladder.)
- While lying or sitting, insert one finger into your vagina and try to squeeze the surrounding muscles. You should feel your finger lifted and squeezed.
- Use a mirror to look at your vaginal opening and perineum (the area between the vagina and rectum) while contracting your pelvic muscles. The perineum should lift up.
- At your next pelvic exam, ask your doctor or nurse to check if you're working the right muscles.

Once you've identified the pelvic floor muscles, you can begin practicing Kegel exercises.

- · Empty your bladder before starting.
- Start by contracting the muscles for three seconds and then relaxing for three seconds. Do 10 repetitions three times a day.
- Lengthen your contraction by one second each week until you're practicing 10-second contractions, with 10 seconds of relaxation in between.
- Do not hold your breath.
- Keep the muscles in your abdomen, buttocks, and thighs relaxed.
- Initially, practice while lying down. As you get stronger, trying practicing while sitting or standing.



Every year, thousands of pregnant women and their partners come to a difficult crossroads.

Told they're at increased risk for having a baby with Down syndrome or another chromosomal disorder, the parents-to-be can elect amniocentesis or chorionic villus sampling (CVS). The prenatal tests are highly accurate at diagnosing some genetic abnormalities, but they pose a risk of miscarriage. Depending on the doctor's level of experience and other factors, the risk can be as high as 1 in 100 or as low as 1 in 1,000, as it is at Magee-Womens Hospital of UPMC.

"You're charged with making this decision about whether to expose your baby to clearly defined risk," says David Peters, PhD, whose lab is developing a safer, noninvasive alternative to amniocentesis and CVS. The former requires inserting a thin needle into the amniotic sac to remove a sample of fluid, while

the latter involves taking a tissue sample from the placenta. Dr. Peters is endeavoring to prove that a simple blood test can be used to diagnose Down syndrome and other abnormalities early in pregnancy.

"Our preliminary data is very, very good," he says. It was good enough for the National Institutes of Health, which awarded him a \$2.8 million grant earlier this year. Dr. Peters, whose

research in noninvasive prenatal testing has been funded by Magee-Womens Research Institute (MWRI) since 2007, will use the five-year grant to collect blood samples from 700 women in the first trimester of pregnancy and apply a new DNA sequencing method to look for extra or missing chromosomes. He expects his noninvasive approach to detect 95 percent of such fetal genetic abnormalities, with a false positive rate of just 1 percent. And the risk of miscarriage? Zilch.

"The overarching goal is to minimize the physical risk to the fetus and minimize the stress to the parents," says Dr. Peters, who is intimately familiar with the stress that can accompany amnio or CVS. He and his wife chose amnio when she was pregnant with their first child at 35 and their second child three years later because the risk of Down syndrome and other chromosomal disorders increases with the mother's age.

"We didn't have a bad outcome from our tests, but we did have a massive amount of anxiety. Minimizing that anxiety would be a major step in the right direction."

His isn't the only MWRI lab looking for ways to minimize the anxiety of parents-to-be. While Dr. Peters pursues an alternative to amnio and CVS, Aleksandar Rajkovic, MD, PhD, is stretching the limits of what we can learn from the procedures.

When a woman undergoes amnio or CVS, the fluid or tissue sample is usually sent to a lab for karyotyping, which involves staining and photographing the fetus's chromosomes, arranging them according to size and banding pattern, and examining them for abnormalities. Down syndrome, for example, is caused by three copies of chromosome 21 instead of the normal two. The problem with karyotyping, says Dr. Rajkovic, is that it doesn't detect smaller genetic changes — some of which cause major problems.

"The overarching goal is to minimize the physical risk to the fetus and minimize the stress to the parents."

- Dr. Peters

Consequently, many parents-to-be who seek amnio or CVS after receiving abnormal ultrasound results are left in the dark. "They want to know what's wrong with their baby, and more than 50 percent of the time, we cannot tell them," Dr. Rajkovic says. "They have to wait until the baby is born to figure out what's going on, which is a huge cause of anxiety."

When Dr. Rajkovic joined MWRI two years ago, he began using chromosomal microarray analysis, a new technology used to look for genetic abnormalities in children born with physical or mental disabilities, to examine samples obtained through amnio or CVS. Scientists isolate the baby's DNA, chop it into tiny pieces, label it with green fluorescent color, and combine it with DNA from a control group that's labeled with red fluorescent color. When they examine the combined samples,

matching DNA pieces appear yellow in color. If the baby is missing a critical part of its genome, the red of the control DNA predominates. "The beauty of this technology is that you don't need to know what you're looking for," Dr. Rajkovic says. "It's especially useful when you're scratching your head because you know there's a genetic problem with the baby, but you don't know what the problem is."

His hunch proved correct: chromosomal microarray analysis uncovers fetal genetic abnormalities missed by karyotyping. "We are able to find reasons for baby's problems in about 10 to 15 percent more cases than with karyotype alone," he says. "It improves our ability to explain to families why their baby is exhibiting anomalies on the ultrasound scan. Knowing the reason removes some of their anxiety."

Chromosomal microarray analysis has been offered to more than 100 women at Magee-Womens Hospital. Because it's not available at most hospitals, Magee's obstetrical geneticists see women from as far away as New York.

Informed Decisions

Medicine has not advanced to the point where most genetic abnormalities can be corrected. But knowing about them has its advantages. Parents-to-be can make an informed decision about continuing or terminating the pregnancy. Those who choose to continue can prepare themselves — emotionally, medically, logistically, and financially — for the journey of raising a child with special needs. Health care providers can prepare themselves for a potentially complicated birth and neonatal problems.

Not long ago, Dr. Rajkovic was asked to evaluate a fetus with a club foot and low amniotic fluid. Each problem is relatively minor, but the combination suggested a genetic abnormality. When the karyotype came back normal, the sample cells were sent to Dr. Rajkovic's lab for chromosomal microarray analysis. The test revealed that the baby carried a small chromosomal deletion called Prader-Willi syndrome, which causes a chronic feeling of hunger that can lead to life-threatening obesity. "It also causes babies to be hypotonic, meaning their muscular tone is very weak, and they have difficulty suckling," Dr. Rajkovic says. "Sometimes people think they have cerebral palsy or brain injury due to trauma during delivery. When the baby came to the NICU [neonatal intensive care unit] and it was hypotonic, the neonatologist didn't have to do a million-dollar workup to figure out why. We saved them from wasting time on trying to figure out what was going on because it was all explained by the fact that this baby had this particular deletion."

Alerting health care providers to genetic abnormalities is a simpler matter than alerting parents-to-be. "These things are not always easy for families to understand, and we spend a lot of time counseling them, explaining what's going to happen after birth and what problems the baby might have," he says.

Magee patients have access not only to world-class obstetrical geneticists like Dr. Rajkovic but also to an experienced team of genetic counselors. Michele Clemens, MS, supervisor of clinical services for the Department of Genetics, has been a genetic counselor for more than 30 years. In that time, ultrasound technology has gotten much better at identifying anomalies, new tests for genetic disorders have been developed, and methods of chromosome analysis have become increasingly sophisticated. "At Magee, we have always been on the forefront or to some degree ahead of the curve," she says.

What hasn't changed is the human factor. Genetic counselors provide critical support to patients before testing, explaining the various tests and the information that can be gained from them, as well as after testing, when emotions can run sky-high. Reactions to bad news are "all over the board," Ms. Clemens says.



"You have patients who are in denial and refuse to accept the result. You have patients who went through testing with the very specific intention of terminating the pregnancy if a problem is identified. And you have those patients in between who struggle with that decision. You even have couples who are discordant in their feelings about what to do. We're there to provide very accurate and clear information about the result, provide a variety of supportive services, and coordinate care if they decide to continue their pregnancy."

Obstetrical geneticists like Dr. Rajkovic envision a future where more and more of the problems caused by genetic abnormalities can be corrected or alleviated. "Diagnosing and understanding the pathologies is the first step," he says. "The question then becomes: can you devise interventions for families that do want to continue the pregnancy? That's the next frontier."

One thing is certain: Magee-Womens Hospital and its eponymous research institute will lead the way. \Box



As the regional referral center for high-risk pregnancies and an otherwise popular place to give birth, Magee-Womens Hospital of UPMC boasts the largest neonatal intensive care unit (NICU) in Pennsylvania. More than 1,000 seriously or critically ill newborns are treated there each year.

Hyagriv Simhan, MD, chief of the Division of Maternal Fetal-Medicine, would like nothing better than to render it useless. "Magee's NICU does a great job," he says. "But my job is to put it out of business."

Dr. Simhan is devoted to solving the riddle of preterm birth, a leading cause of infant death, illness, and disability. Each year in the United States, more than

half a million babies are born before reaching full term, or 37 weeks of gestation. The odds of giving birth prematurely are 1 in 8 — about the same as a woman's lifetime risk of invasive breast cancer.

Like cancer care, prematurity care has come a long way in recent decades. Thanks to NICUs like Magee's, the vast majority of preterm births aren't

death sentences. In 1963, the youngest child of President John F. Kennedy and First Lady Jacqueline Kennedy was born about five weeks early and died of respiratory failure two days later. Had he been born today, the technologies of the NICU almost certainly would have saved his life. That's the good news. Here's the bad: While mortality in premature infants has fallen sharply, the rate of preterm births in the United States has not. In fact, it rose by more than one-third from 1981 to 2006, when it began a modest decline attributed to a new hormonal treatment for women with a history of preterm delivery. Researchers and doctors are still struggling to understand what causes women to give birth prematurely. "We haven't found a smoking gun," says Steve Caritis, MD, who preceded Dr. Simhan as chief of maternal-fetal medicine and has been studying prematurity since the mid-1970s. Consequently, they can't predict which women will deliver prematurely.

You wouldn't blame them for throwing in the towel. Instead, Drs. Simhan and Caritis and scientists at Magee-Womens Research Institute (MWRI) have a decidedly sunny outlook. "The skeptic may say, 'Jeez, you guys haven't done anything over the last 40 years,' but I think we're closer now than we've ever been," Dr. Caritis says. "We have a better understanding of preterm birth than ever before. We never had a medication or treatment that actually reduced prematurity rates and improved perinatal outcome, but now with progesterone supplementation, we have a treatment that has proven effective in reducing preterm delivery in certain high-risk women. So our understanding of preterm birth and its causes and treatments is increasing fairly rapidly, and with molecular techniques, it will get even faster."

Magee is uniquely poised to make the next breakthroughs. "We have experts in many key areas of prematurity," Dr. Caritis says. "There are very few places in the

Each year, there are more than half a million preterm births in the United States and more than half a million preterm-related deaths in the world.

country that have this many investigators focusing on prematurity." In addition to Drs. Caritis and Simhan, who are internationally recognized experts on labor-inhibiting drugs, the team includes Jennifer Condon-Jeyasuria, PhD, whose lab has identified a cellular protein that appears to keep the uterus from contracting, and Lisa Bodnar, PhD, MPH, RD, whose research focuses on the impact of maternal nutrition on birth outcomes.

The volume of births at Magee and its experience in grand-scale scientific studies also distinguishes it from other institutions, says Dr. Simhan. "We are unique because we have this tradition of being able to do clinical and biological research in large groups of women. The fact that we can extend that research to the newborn and infant period and beyond is truly unparalleled, and what we discover will help prevent the consequences of prematurity for children all over the world."

The Progesterone Puzzle

The year 2003 marked a watershed in the war against preterm birth. A multicenter research network that included Magee released the results of a clinical trial on the effects of a drug called 17 alpha-hydroxyprogesterone caproate (17-OHPC) on pregnant women with a history of spontaneous preterm delivery. The researchers found that weekly injections of the naturally occurring hormone reduced preterm birth by 34 percent. And infants of women treated with 17-OHPC had significantly lower rates of several complications associated with prematurity. In response, the American College of Obstetricians and Gynecologists endorsed the use of 17-OHPC to prevent recurrent preterm delivery. After decades of research and failed treatments, ob-gyns finally had a proven prevention strategy.

Separate trials have shown that administering progesterone by vaginal suppository greatly reduces the rate of preterm deliveries in women with a short cervix.

"We know progesterone supplementation works, but we don't know why it works," says Dr. Caritis, who helped lead the groundbreaking study on 17-OHPC injections. He's now intent on answering that question. Understanding how progesterone levels affect the timing of labor could lead to further treatments for preterm birth.

Dr. Condon-Jeyasuria may have found part of the answer. Her research suggests that progesterone regulates a cellular protein called caspase-3, which robs uterine muscle cells of their ability to contract. Caspase-3 levels in the uterus soar in the earlier months of pregnancy and taper off in the later months. When the protein disappears, the muscle cells regain their ability to contract, setting up the conditions for labor. "Nobody had looked at caspase-3 and its effect on the uterus," says Dr. Condon-Jeyasuria, whose trailblazing was rewarded with a \$475,000 grant from the March of Dimes and a five-year \$1.5 million grant from the National Institutes of Health.

She believes her lab's unorthodox approach to the study of preterm birth helped it snag the sizeable awards. "A lot of researchers are trying to identify the silver bullet that causes the uterus to suddenly contract. We've taken a different tack: Why doesn't the uterus contract all the time? Why doesn't preterm birth happen more often? Why is it only 1 in 8

pregnancies? There has to be something stopping the uterus from contracting throughout the whole of pregnancy. So we're focusing on identifying the factors that maintain quiescence. Maybe it's the loss of these factors, rather than some silver bullet, that triggers birth."

The Holy Grail

Magee's Center for Prematurity, which opened in 2002, provides specialized care to women at high risk for preterm delivery, primarily women with a history of giving birth prematurely. In addition to progesterone supplementation, it offers infection screenings, ultrasounds to detect changes in the cervix, and cervical cerclage (a surgical procedure in which the uterus is stitched closed). "Our approach is to prevent prematurity if we can, and even if we can't, to prolong pregnancy and

Preterm birth is expensive.
In the United States, the average hospital charge for preterm newborns is \$77,000, compared to \$1,700 for term newborns.

improve outcomes for the baby," Dr. Simhan says.

The approach significantly reduces recurrences. But high-risk clinics can't make a major dent in the national preterm birth rate. That's because most women who deliver prematurely have no reason to suspect that they will. "Most preterm births are first preterm births," Dr. Simhan explains. "We do not have effective screening and prevention strategies for women without a history of preterm delivery. That's the holy grail."

A new multicenter study may help him find that holy grail. Dr. Simhan is among the principal investigators for the

Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be (nuMoM2b), established by the National Institute of Child Health and Human Development. Researchers will collect data from 10,000 women who are having their first baby and will look for predictors of preterm birth and other adverse pregnancy outcomes.

Dr. Simhan is particularly interested in how nutritional status influences the mother's immune system and her risk of preterm delivery. He and Dr. Bodnar, an epidemiologist, coauthored a study showing that pregnant women with low levels of vitamin D may be more likely to suffer from bacterial vaginosis, a common infection associated with preterm birth. Vitamin D, which is naturally present in very few foods, is produced by the body in response to sun exposure. "Pittsburgh is one of the grayest cities in America," Dr. Simhan notes. "We have a huge frequency of vitamin D deficiency." The connection between vitamin D and

There are two main types of preterm births. Most preterm births are "spontaneous," occurring as a result of preterm labor or premature rupture of the amniotic sac. About 25 percent of premature births are "indicated," or initiated by health care providers due to problems such as preeclampsia or placental bleeding.

vaginosis may be one reason why African-American women, who need more sunlight than lighter-skinned women to generate the same amount of vitamin D, are more prone to the infection and nearly twice as likely to give birth prematurely.

A deeper understanding of how vitamin D, folate, and other nutrients relate to preterm birth is needed before health care providers can recommend supplementation, he says. "It would be irresponsible to take the data that we have right now and say 'Check your level of this or supplement that.' There is no ready-for-primetime nutritional intervention." For now, his best advice is that women eat a healthy diet, maintain a healthy weight, and begin taking prenatal vitamins before they become pregnant.

He also advises that women heed the signs of preterm labor. "If you're having contractions, bleeding, leak of fluid, or abnormal vaginal discharge, go get examined — even if it's inconvenient, even if it's 2 in the morning — because that's how preterm birth presents for many women. Most women with those symptoms are fine, but you don't know that unless you get checked out."

Ultimately, Dr. Simhan hopes to do more than put NICUs out of business. Preventing preterm birth reduces not only the number of sick babies but also the number of sick kids, teens, and adults. That's because prematurity can have long-term consequences, including learning and behavioral problems, cerebral palsy, vision and hearing loss, and increased risk of obesity, diabetes, high blood pressure, and heart disease. "The benefits of preventing preterm birth are huge," he says. "From a public health perspective, if you can improve the health of a baby, that's 85 years of health outcome."

Three groups of women are at greatest risk for preterm delivery: women with a prior preterm delivery, women carrying more than one fetus, and women with certain uterine or cervical abnormalities.

Babies born between 37 and 42 weeks of gestation are considered full term. Those born before 37 weeks are considered preterm, or premature.



GWMG IN ACTION



MWRIF Chairwoman: Giving has Endless Rewards

Thanks to humanitarians like Margaret "Peggy" Joy, chairwoman of the Magee-Womens Research

Institute & Foundation (MWRIF) board of directors, the future of medical research and education in Pittsburgh is bright.

A partner in the family law firm McCarthy McDonald Schulberg & Joy, Peggy has made numerous gifts totaling more than \$87,000 in support of an annual lectureship at the research institute, many hospital and research projects, nursing education, and various fundraising events. The lectureship is geared toward young scientists and affords them an opportunity to interact with distinguished researchers from throughout the UPMC system and other institutions. The first annual Margaret P. Joy Research Day Lecture was held in June 2010.

Like many MWRIF supporters, Peggy first interacted with Magee-Womens Hospital of UPMC as a patient. "My initial interest in Magee was the wonderful medical treatment I received in connection with some surgeries and treatment I had when I was in my 20s, and then later for the birth of my daughter. I can now also celebrate the birth of my beautiful grandson in July 2010, with another grandchild on the way," she says.

Peggy became involved with the MWRIF board in the late 1990s, when the research institute was undergoing its initial growth period. "I was inspired by the concept of a research institute so closely connected with a top-flight clinical hospital specializing in women's and infants' health issues," she explains.

Peggy believes she has gained as much as, if not more than, she's given. "The rewards to the donor in supporting things you are passionate about are endless. They contribute to a rich life and fulfill a sense of responsibility that we all should have toward those issues and problems in our world that we can impact, in whatever ways we have available to us. I have loved working with the dedicated community volunteers, all leaders in their own worlds, who care so much about Magee and the patients we serve every day."

- Jamie Loveland & Andrea Romo

Grateful Parents Raise \$80,000 Toward Fight Against Prematurity

Sam and Alyssa Robb Tell Their Story

The miracle of life: It's not an overused expression to us. It's an absolute truth. For we have experienced it firsthand, with our son Baylor, who was born at 26 weeks. Arriving far too early and much too tiny at just over 2 pounds, he spent 75 days in the neonatal intensive care unit. Miraculously, he has grown into a healthy, happy toddler.

Sadly, like so many other parents, we have also experienced the tragedy of loss. Our son Hudson, Baylor's twin brother, survived just 36 hours. And prior to that, we lost a daughter, Logan, at 23 weeks. While our devastation seemed insurmountable at the time, we were thrown a lifeline by an incredible physician, Dr. Hyagriv Simhan at Magee-Womens Hospital of UPMC. He and his team in the Division of Maternal Fetal Medicine not only comforted and encouraged us in our dark days, they brought light to our lives by helping us move forward.

Now it is our turn to help Dr. Simhan conduct vital research to battle prematurity. With more than half a million babies born prematurely in the United States each year, the combined toll of dashed hopes, lost lives, and skyrocketing medical expenses is difficult to fathom. It is our mission to make that number zero.

[Soon after delivering Baylor and Hudson, the Robbs wanted to know what they could do to show their gratitude to Magee for giving them the opportunity to have a family. Working with Dr. Simhan and Magee-Womens Foundation, the Robbs hosted the Fight Prematurity Benefit at The Club at Nevillewood in September. The event attracted 200 guests and raised \$80,000 toward the purchase of a PEA POD®, a state-of-the-art piece of equipment used in preterm birth research.]

We are thrilled with the results of this event, but this is just the start of our work with Magee. We understand that research is critical to reducing preterm births and other pregnancy complications. We are making a lifelong commitment to do what we can to fight prematurity, and we hope others will join us. Dr. Simhan and his research and clinical team at Magee are passionate about what they do, and we are too.

- A.R. , Sam and Alyssa Robb

Family and Friends Honor Memory of Rod Rogerson Through Philanthropy

Whenever respiratory therapist Rod Rogerson lost a patient, he would walk past the newborn babies in the hospital to remind himself that when a life is lost, a new one begins. Later, he became a global trainer for Phillips Children's Medical Ventures, which develops newborn care products. When he passed away on May 31, 2010, his family and friends decided to continue his legacy of supporting newborn care. They raised \$22,170 for a state-of-the-art incubator for the neonatal intensive care unit (NICU) at Magee-Womens Hospital of UPMC.

In June, Rod's family and friends gathered to celebrate the purchase of the Giraffe® incubator. "The Giraffe bed incorporates advanced technology with easy accessibility to allow the nurses to provide quality care in a healing environment," says Karen Ewing, NICU unit director. "The bed is adaptable to various heights to accommodate all caregivers and has many doors for easy access."

The money raised in Rod's memory also funded the ninth annual Women and Infants Health Care Conference. Held at Magee-Womens Hospital, the conference focuses on the latest treatments and technologies in maternal-infant health care.

Rod has touched the lives of many children and families, and his hard work will live on. His closest friends — Bill Andrews, Terry O'Day, and Greg Trusivich — will always remember Rod's dedication to giving premature babies the chance to grow into healthy children.

-A.R.

Twins' Birthday Party Raises \$1,500 for Magee's NICU

Donald and Laura Albensi faced the unexpected with the birth of their first children, twin boys Devin and Kieran, when Laura's water broke 10 weeks before her due date. She assumed the babies were "wreaking havoc" on her bladder and didn't seek care immediately. Fortunately, she had a regular prenatal checkup the next day and was sent directly to Magee-Womens Hospital of UPMC. Three days later, she was in labor.

The twins were born on August 25, 2010, both weighing just over 2.5 lbs, and were whisked away to Magee's neonatal intensive care unit (NICU).

Two days later, Donald and Laura were finally able to hold their fragile babies outside of their incubators. Kieran and Devan were in the NICU for 42 and 47 days, respectively. They faced many complications, including underdeveloped lungs, breathing problems, jaundice, and many episodes of apnea and bradycardia. Kieran had a small hole in his heart that thankfully resolved itself after several months.

Recently, the twins celebrated their first birthday. The Albensi family requested donations to Magee's NICU in lieu of gifts and raised \$1,500. "The boys were blessed with so many gifts from our wonderful family, friends, and employees during their first year, so we thought this would be a great opportunity to give back to the NICU," Laura says.

Today, the twins are happy and healthy and on the verge of walking. You might never guess they arrived too soon.

-A.R.

Wedding Reception Doubles as Fundraiser

Ever since she was 14, Nicole Kashmer has suffered from endometriosis and adenomyosis, both complications of the reproductive system. After enduring pain and surgeries and bouncing from physician to physician, Nicole was referred to Magee-Womens Hospital of UPMC, where she finally found the support and care she was seeking. Michael Stepek, her longtime friend and now husband, helped Nicole through these difficult and painful times, and they wanted to show their appreciation to Magee.

On August 27, the couple wed at Old St. Luke's in Carnegie, Pennsylvania. On September 3, they hosted a reception for about 100 people at Groveton Park in Robinson Township, Pennsylvania. Already blessed with plenty of "stuff," the couple asked guests to make donations to Magee-Womens Foundation in lieu of gifts. They raised \$515.

"Our marriage represents so much more than I could ever put into words," says Nicole, who has an 8-year-old son, John. "I do not know if I will be lucky enough to have any more children, but either way, I feel so blessed to have the husband that I do, and I was determined to give back."

-A.R.

OUR DONORS

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Every attempt has been made to ensure the accuracy of this list. If you find an error or omission, please contact Jean Nelson-Sims at 412.641.8968 or nelsonsimsrj@mwri.magee.edu.

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In honor of Connor

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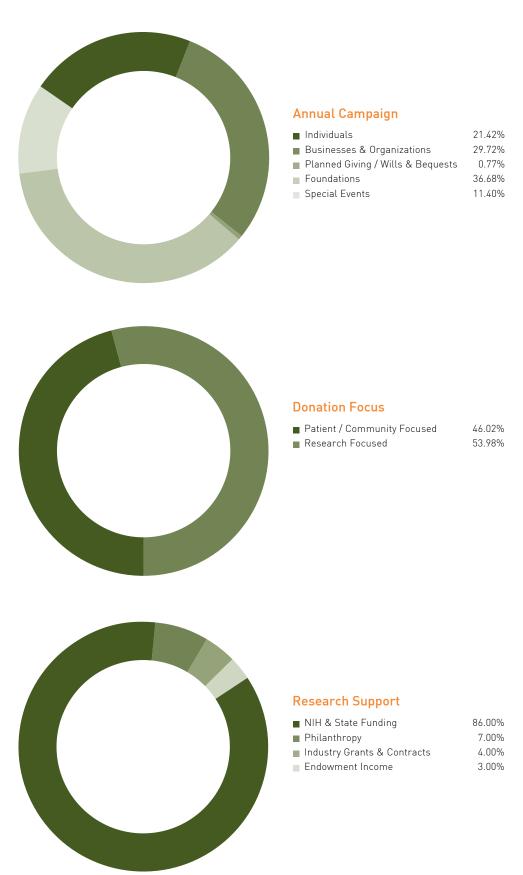
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FY11 Financial Overview



Events / Happenings

DECEMBER

[DECEMBER 1-20]



Various in-house sales, including Fudgie Wudgie Sale, Aunt Carol's Gourmet Dips Sale, Popcorn-N-That Sale, Arbonne Products, Beth's Beads & Denim Designs by Jeanene, and Pretzel Crazy Sale

Where: Magee-Womens Hospital of UPMC

When: 7 a.m. to 4 p.m./5 p.m.

Proceeds benefit Girls on the Run at Magee or the Julene Fabrizio Ovarian Caner Research Fund.

For more information, visit www.mwrif.org/calendar.

[DECEMBER 18]



Jim Henderson hosts the sixth annual Freeze Your (Golf) Balls Classic

Where: South Hills Country Club (Whitehall, PA)

Proceeds benefit breast cancer research.

For more information and to register, please contact Jim at henderson@duq.edu or 412.418.1924.

FEBRUARY

[FEBRUARY 15-17]



Magee on the Road in Florida

Where: Naples and West Palm Beach, Florida

For more information, please contact Colleen Gaughan, Magee-Womens Foundation, at cgaughan@magee.edu or 412.641.8978.

MAY



[MAY 25]

Research Day in Reproductive Biology and Women's Health

Where: Magee-Womens Hospital of UPMC, Auditorium [Oakland, PA]

For more information, please contact Colleen Gaughan, Magee-Womens Foundation, at cgaughan@magee.edu or 412.641.8978.

JUNE

[JUNE 3]



Annual NICU Reunion

Where: Pittsburgh Zoo & PPG Aquarium (Highland Park, PA)

Proceeds benefit the neonatal intensive care unit.

For more information, visit www.mwrif.org/calendar.

[JUNE 15]



Department of Obstetrics, Gynecology & Reproductive Sciences Awards Ceremony

For more information, please contact Colleen Gaughan, Magee-Womens Foundation, at cgaughan@magee.edu or 412.641.8978.

NICU Reunion



2005 at Kennywood



2011 at the Pittsburgh Zoo & PPG Aquarium

This year's NICU Reunion attracted a record number of children who graduated from Magee's neonatal intensive care unit.

The Magee Society



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The Magee Society provides a unique opportunity for an elite group of donors who contribute \$500 or more annually. Each leadership gift helps to ensure that the compassionate spirit of our founding donor, Christopher Magee, will live on.

Members of the Magee Society help Magee-Womens Hospital and Magee-Womens Research Institute provide the most highly developed medical care, fund the needs of patients and advance our cutting-edge research on women's health issues.

We invite you to join this passionate group of people this year as Magee celebrates its 100th anniversary! For more information, visit www.mwrif.org or contact Colleen Gaughan, director of development, Magee-Womens Foundation, at 412-641-8978 or cgaughan@magee.edu.

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